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Free Radical Additions to Cis-Cyclooctene and Cis-Cyclodecene.

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FREE RADICAL ADDITIONS TO CIS-CYCLOOCTENE AND CIS-CYCLODECENE

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ABSTRACT

Free radical additions to cis-cyclooctene and cis-cyclodecene were investigated to determine if transannular additions accompany such reactions. Both normal and transannular additions occur, depending mainly upon the nature of the addend. Photo- and thermally-initiated additions of carbon tetrachloride give principally an isomeric mixture of 1-chloro-4-trichloromethylcyclooctanes. The transannular nature of these products was proven by selective dehydrochlorination of both isomers to the same 1-chloro-4-dichloromethylenecyclooctane, which, through ozonation was converted to 4-chlorocyclooctanone.

The addition of trichloromethanesulfonyl chloride gives substantial amounts of 1-chloro-2-trichloromethylcyclooctane in addition to the transannular products. Addition of bromotrichloromethane gives principally 1-bromo-2-trichloromethylcyclooctane with minor amounts of the 1,4 isomers.

Chlorinations of cyclooctene and cyclodecene give the 1,2-dichlorocycloalkanes as the only addition products under both ionic and free radical conditions.

The competition between vicinal and transannular addition is discussed in terms of the kinetic and energy requirements for the two processes.

CHAPTER I

INTRODUCTION

Medium ring compounds (those of ring size eight to twelve carbon atoms) exhibit certain chemical and physical properties which set them apart from other ring sizes.[1] Thermochemical measurements indicate that these rings are unusually strained[2] and X-ray data[3] show considerable deviation from the tetrahedral valence angle. A major source of this strain is the end-on interaction of the hydrogens on opposite sides of the ring (transannular strain). Cope[4] suggests the use of the term "proximity effect" to include other non-vicinal interactions in which an atom or group is fixed in the proximity of another group by steric requirements of the molecule. Because of this closeness (or proximity), it is possible for usually inert groups to participate in a reaction occurring three or more carbon atoms away. If this participation involves migration of an atom or group, it may be classified as a transannular rearrangement.

For medium rings, the migration of a hydride ion to a transannular carbonium ion site has been most extensively studied.[1,4] The first observations of transannular hydride migrations were reported almost simultaneously by Cope[5] and Prelog[6] in the peroxyformic acid oxidations of cyclooctene

and cyclodecene. Medium ring olefins give little or none of the expected 1,2-diols; the 1,4-, 1,5-, and 1,6-diols are obtained from cyclooctene, cyclononene, and cyclodecene, respectively.[1] Since these initial investigations, numerous examples of transannular hydride migrations have been reported.

In contrast, few data have been reported concerning the analogous hydrogen atom migration to a transannular free radical site. This present work is concerned with this question.

Among several possible methods of generating a free radical on a medium ring, addition to an olefin seemed the most promising for this type of study. The free radical addition of an addend A-B to an olefin has been shown to occur in several steps:[7]

(1) initiation: $A\text{-}B \xrightarrow[\text{light}]{\text{heat}} A\cdot + B\cdot$

or: $In_2 \xrightarrow{\text{heat}} 2In\cdot$

Where In_2 represents an "initiator" such as benzoyl peroxide.

$In\cdot + A\text{-}B \longrightarrow In\text{-}B + A\cdot$

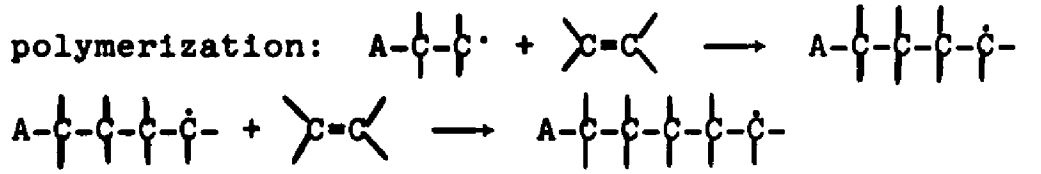
(2) addition: $A\cdot + \rangle C{=}C\langle \longrightarrow A\text{-}\overset{|}{C}\text{-}\overset{|}{C}\cdot$

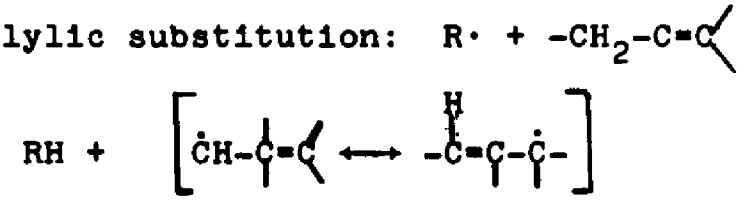
(3) chain transfer: $A\text{-}\overset{|}{C}\text{-}\overset{|}{C}\cdot + B\text{-}A \longrightarrow A\text{-}\overset{|}{C}\text{-}\overset{|}{C}\text{-}B + A\cdot$

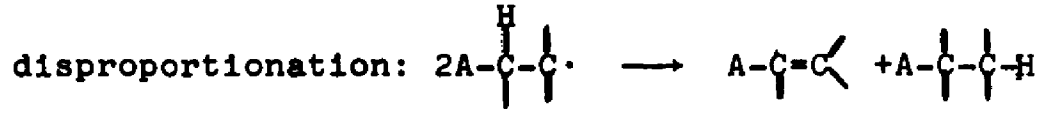
In principle, introduction of a single free radical in the initiation step (1) may cause hundreds or even thousands

of molecules to react since the radical A· is reformed in the chain transfer step. Actually this simple scheme is always complicated by the competing reactions listed below:

(4) dimerization: $R\cdot + R'\cdot \longrightarrow R\text{-}R'$

(5) polymerization: 

(6) allylic substitution: 

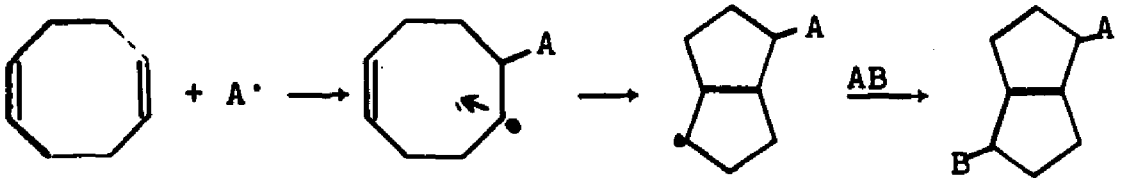
(7) disproportionation: 

By proper choice of experimental conditions the addition reaction can usually be made to predominate over polymerization and allylic substitution.

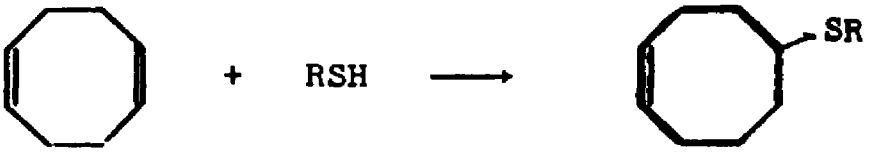
Addition of an addend to an olefin under free radical conditions is usually accompanied by the several reactions typical of a free radical: dimerization, abstraction and disproportionation. Therefore, one can assume that a free radical intermediate is formed in the addition reaction and that its rearrangement may be studied by examination of the products formed from such an addition.

The related problem of a transannular free radical ring closure (involving the transannular migration of an unpaired electron) has been studied by several workers.

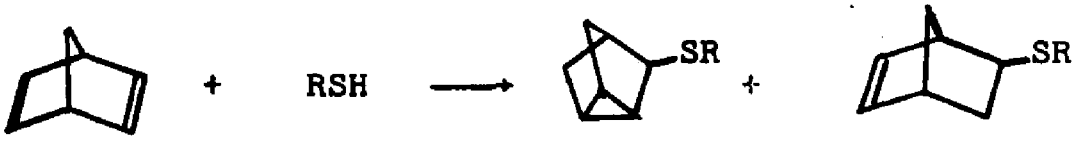
Dowbenko reports that free radical additions to 1,5-cyclooctadiene yield principally substituted bicyclo[3.3.0]octanes by way of a transannular mechanism.[8]



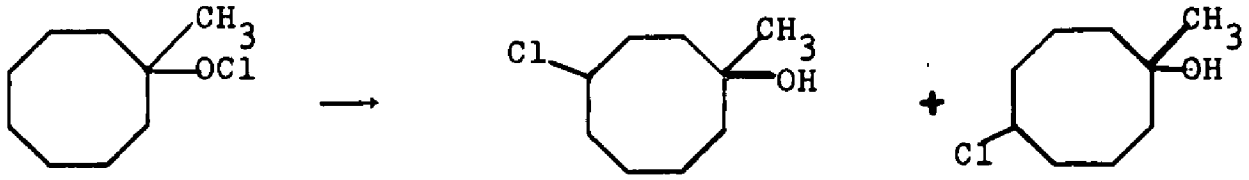
Although the author claims this reaction is quite general, free radical additions of certain thiols are reported to give only the normal 1,2 addition products.[9]



Similar competition between normal addition and transannular ring closure has been reported in the related norbornadiene system.[10]

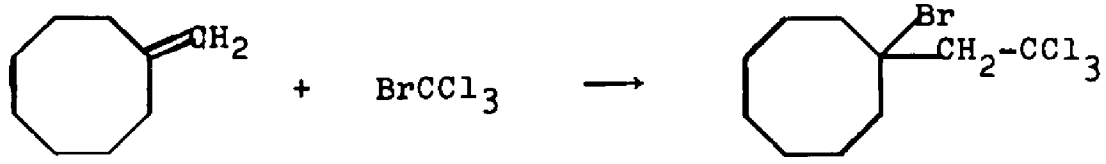


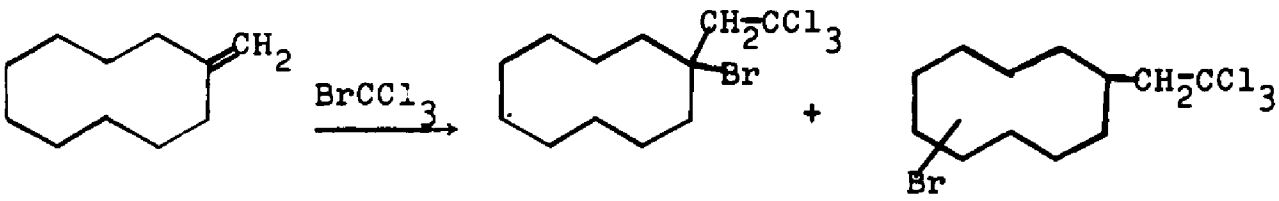
A recent paper reports transannular hydrogen atom abstraction by an oxygen radical formed in the decomposition of 1-methylcyclooctyl hypochlorite.[11]



The mechanism for this reaction is pictured as the homolytic breaking of the O-Cl bond, a transannular hydrogen abstraction by oxygen, and finally, intermolecular chlorine abstraction (by the carbon in position 4 or 5) to regenerate the oxygen radical and continue the chain.

A few months ago, Fisch and Ourisson reported that addition of bromotrichloromethane to methylenecyclodecane gives both the normal (vicinal) and transannular product.[12] The structure of the transannular product was not established but its n.m.r. spectrum (a quintet for H-C-Br) clearly differentiates it from the normal product, which contains a tertiary bromine. The authors also report that the addition of bromotrichloromethane to methylenecyclooctane gives only the normal product.[12]





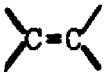
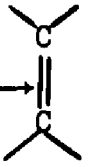
In the methylenecyclodecane reaction, a tertiary free radical apparently rearranges to a secondary free radical. The authors have designed their experiment in exactly this fashion to exclude an ionic rearrangement, which would require a change from a tertiary to a secondary carbonium ion.

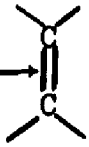
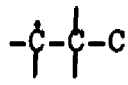
Although the factors which stabilize a free radical are not well understood, they apparently closely parallel the carbonium ion case. For example, the stabilization energies of the methyl, ethyl, isopropyl and t-butyl radicals are 0, 4, 8, and 12 Kcal./mole, respectively.[13] Thus, the destabilization of the tertiary radical by the adjacent trichloromethyl group must outweigh the stabilization energy (approximately 4 Kcal./mole) lost in the rearrangement to a secondary radical.

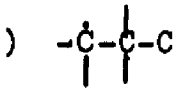
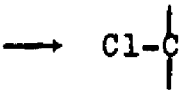
In the present work, free radical additions to cyclooctene and cyclodecene have been studied. The intermediate radical was secondary and the rearranged radical was also secondary.

If "X" is an electron-withdrawing substituent (such as trichloromethyl) the primary radical will be destabilized with respect to the rearranged radical. In spite of this favorable free energy difference between the initial and rearranged radical, rearrangement (by way of a transannular hydrogen atom shift) will not take place unless the rate of this rearrangement is fast compared with competing processes. The proportion of 1,2 and transannular products will depend on the relative rate at which the initial radical reacts with the addend compared to the rate of transannular rearrangement.

The addends used in this work were of two types, polyhalomethanes and chlorine. The former react by the mechanism outlined earlier in this discussion. Chlorine addition to olefins follows a somewhat different mechanism and requires further discussion. Free radical addition of chlorine to olefins needs no external initiation and occurs even in the dark at -70^{o}.[14b] The initiation (or production of primary radicals) occurs by a process known as "induced homolysis."[15] The interaction of the chlorine with the olefin is believed to occur in the following manner:

(8) Cl_2 +  ⟶ Cl_2  (molecular complex)

(9) Cl_2  +  ⟶ 2 

(10)  + Cl_2 ⟶  + Cl·

Equation (9) represents the initiation step and need not occur frequently in order for a very large number of molecules to react. Note that a chlorine atom is produced in equation (10); this atom can add to the olefin to produce the same radical formed in equation (9).

Alkanes are inert to chlorine at -70° in the dark.[14b] However, if an alkane is used as a solvent in the chlorination of an olefin, hydrogen is abstracted from the solvent giving the chlorinated hydrocarbon.[14b] This reaction provides strong evidence for both the free radical nature of the addition and the idea of induced homolysis.

Chlorination of olefins can also proceed by an ionic mechanism.[14b,c,d] If oxygen is introduced into the reaction mixture, evidence for a free radical mechanism (such as the hydrogen abstraction mentioned above) is not observed, but the addition of chlorine to the double bond still proceeds at a rapid rate.

In spite of the dual mechanisms for the chlorination of olefins, the free radical mechanism can usually be made to predominate if the olefin is in high concentration (preferably neat) and oxygen is rigorously excluded from the system. Conversely, the ionic mechanism predominates in dilute solutions of the olefin, in polar solvents, and in the presence of a large excess of oxygen.[14b,d]

In this work, chlorinations were carried out under both ionic and free radical conditions.

CHAPTER II

RESULTS AND DISCUSSION

Product distribution data were obtained for the free radical additions of CCl_4, $BrCCl_3$, CCl_3SO_2Cl, and Cl_2 to cis-cyclooctene, and for Cl_2 and CCl_4 additions to cis-cyclodecene.

The products from the above reactions were isolated by procedures outlined in the experimental section and their structures were established by degradation, independent synthesis, infrared and n.m.r. spectroscopy, and comparison with authentic samples. The quoted yields of the major addition products generally represent the quantity actually isolated, while some of the yields of the minor products were obtained from gas chromatographic data and are uncorrected for possible differences in their relative response to the flame ionization detector.

A simple correlation between the position of substitution on the cyclooctane ring and the n.m.r. spectrum of these products was observed and seems to be quite general. Because of the importance of the n.m.r. method for determination of structure in this system, the general method will be summarized here.[16] The method depends on the fact that the deshielding effect of the electron withdrawing groups decreases rapidly with distance so that protons separated by

four chemical bonds from a deshielding group (A protons) are unaffected. Protons separated by three chemical bonds (B protons) show a small shift while protons separated by two chemical bonds (i.e., on the same carbon atom, C protons) show the largest shift. Typical examples of these types of protons follow: (where X = CCl_3, Cl, Br, OH)

A protons (-1.65 p.p.m.*)	$-CH_2-\underline{C}H_2-CH_2-$
B protons (-2.4 to -1.8 p.p.m.)	$C\underline{H}_2-C-X$
	$C\underline{H}_2-C\equiv C$
	$C\underline{H}_2-C=O$
C protons (-6.0 to -2.5 p.p.m.)	$\underline{H}-C-X$
	$\underline{H}-C\equiv C$

*Throughout this dissertation, all chemical shifts will be given relative to tetramethylsilane internal reference.

TABLE I

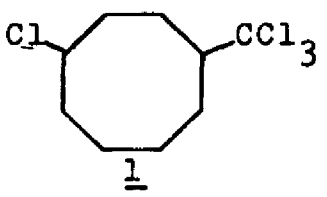
CORRELATION OF N.M.R. SPECTRA WITH POSITION OF SUBSTITUTION FOR CYCLOOCTANE DERIVATIVES

Type of Substitution	Integrated absorption		
	A	B	C
Unsubstituted	16	0	0
Monosubstituted	10	4	1
Mono-olefin			
endo	8	4	2
exo	10	4	0-2[a]
Diolefin			
1,3	4	4	4
1,4	2	6	4
1,5	0	8	4
Disubstitution			
1,2	8	4	2
1,3	6	6	2
1,4	4	8	2
1,5	4	8	2
Endo-olefin, Monosubstitution			
1-X-1-ene	8	4	1
3-X-1-ene	6	4	3
4-X-1-ene	4	6	3
5-X-1-ene	2	8	3
Exo-olefin or Ketone, Monosubstitution			
1,2	8	4	1-3[a]
1,3	6	6	1-3
1,4	4	8	1-3
1,5	4	8	1-3

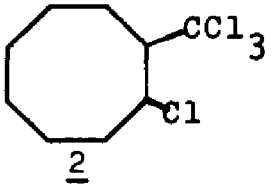
[a]The number of C protons depends on the substitution at the exo vinyl positions. In this work, only dichloromethylenes were involved, and the minimum number cited is appropiate.

TABLE II

PRODUCT DISTRIBUTION DATA FOR CCl_4 ADDITIONS TO CIS-CYCLOOCTENE



1



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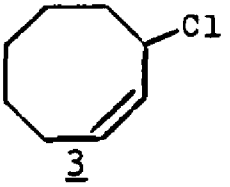

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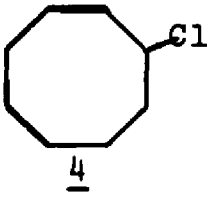

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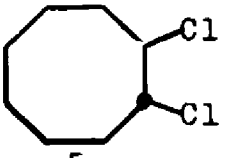

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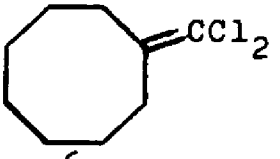

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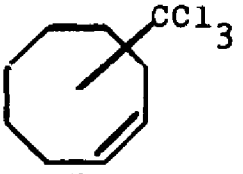

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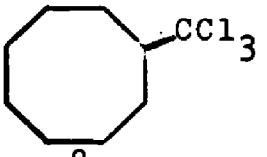


8

CCl_3-CCl_3
9

Others Unidentified
10

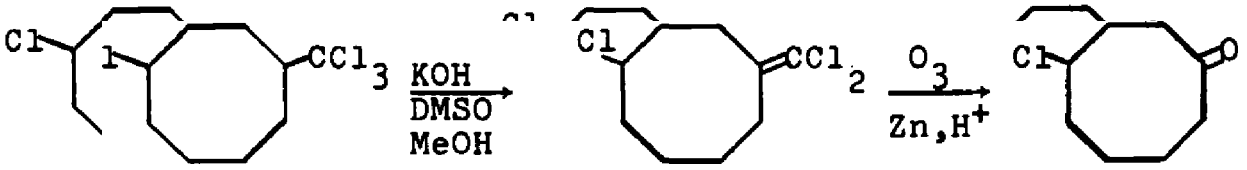
	Yield, Mole %									
Conditions[a]	1[b]	2[b]	3	4	5	6	7	8	9	10[c]
Photoinitiated	67	3.8	.71	.61	1.3	2.6	3.4	5.0	.07	3.0
Thermally-initiated	58	1.2	.89	8.2	1.2	.36	8.0	.30	.07	5.1
Photoinitiated in benzene solution	66	5.0	.13	1.1	1.7	5.1	1.5	.89	.89	3.3
CCl_3SO_2Cl addition	56	25	.05	.16	1.0	1.3	1.0	.08	.08	4.3

[a]See Experimental for details. [b]Both cis and trans isomers were obtained. [c]These figures exclude polymer and undistillable material.

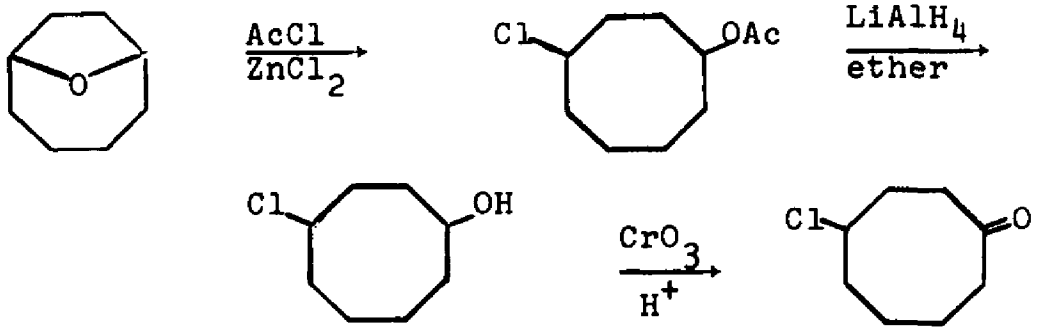
A. Carbon Tetrachloride Additions

1. Results

Addition of carbon tetrachloride to cis-cyclooctene gives principally a cis-trans mixture of 1-chloro-4-trichloromethylcyclooctanes. The structures of these products were proven by degradation to 4-chlorocyclooctanone by the following sequence of reactions:



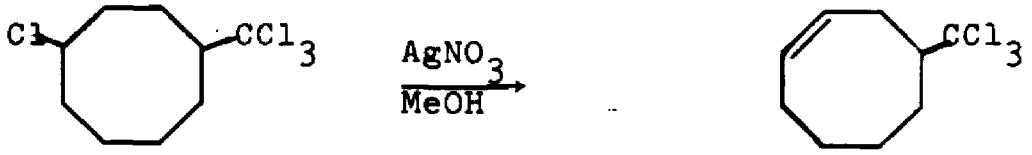
The same dichloromethylenechlorocyclooctane was formed from each of the major products or from a mixture of them, confirming their geometrical isomerization. The identity of the previously unreported 4-chlorocyclooctanone was established by the following synthesis:



By an identical scheme, 5-chlorocyclooctanone was synthesized from 9-oxabicyclo[3.3.1]nonane[17] and shown to be absent from the product mixture obtained from the ozonation of

1-chloro-4-dichloromethylenecyclooctane. Thus, little or no 1,5 addition of CCl_4 to cyclooctene could have occurred.

The transannular nature of the major addition products is also supported by the dehydrochlorination of each of the two isomers with alcoholic silver nitrate to give a high yield of 4-trichloromethylcyclooctene.



The formation of this product is not definite proof of the structure of the original addition compound since a transannular ionic rearrangement of an intermediate 2-trichloromethylcyclooctyl cation (via a hydride shift) could have given the same product.

The free radical addition of trichloromethanesulfonyl chloride may be classified as a carbon tetrachloride addition since sulfur dioxide is lost and the elements of CCl_4 are added to the olefin. The important difference between these two reagents is the rate at which chlorine is abstracted by a free radical species. Chlorine is abstracted from the sulfonyl chloride at a substantially faster rate than from carbon tetrachloride.[18,13]

The relative rates of chlorine abstraction from these two reagents is illustrated by the fact that CCl_3SO_2Cl

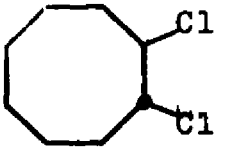
gives a 1:1 addition product with styrene while carbon tetrachloride gives only low molecular weight polymers.[18]

In addition to a 56% yield of 1-chloro-4-trichloromethylcyclooctanes (19% solid and 37% liquid isomer) and several minor products, 1-chloro-2-trichloromethylcyclooctane was isolated (in 25% yield) from the addition of CCl_3SO_2Cl to cis-cyclooctene. The structure of the 1,2 isomer was established by n.m.r. spectroscopy (the A:B:C ratio was 8:4:2). Reexamination of the other carbon tetrachloride addition mixtures revealed that 1-chloro-2-trichloromethylcyclooctane was formed to the extent of 1.5 - 5%.

In all of the carbon tetrachloride addition reactions a variety of lower-boiling products (1 to 3 chlorines per C_8 or C_9 group) was formed. The distributions of these minor products were quite similar among the different runs and, in general, were not helpful in the understanding of the addition mechanism. The nature and variety of these products underscores the free radical nature of these additions. The formation of hexachloroethane and trans-1,2-dichlorocyclooctane gives evidence for the dimerization of $CCl_3\cdot$ and $Cl\cdot$ radicals.

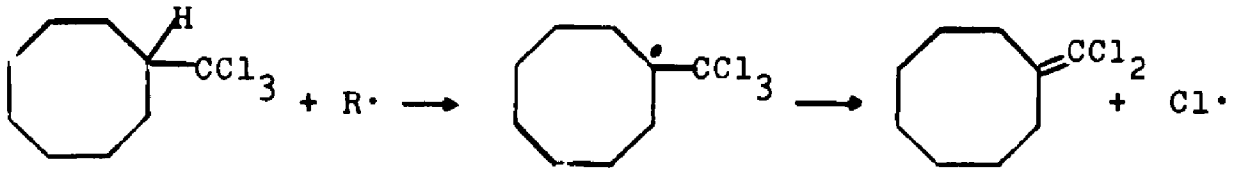
$$2CCl_3\cdot \longrightarrow CCl_3\text{-}CCl_3$$

$$2Cl\cdot \longrightarrow Cl_2 \xrightarrow{\text{cyclooctene}}$$

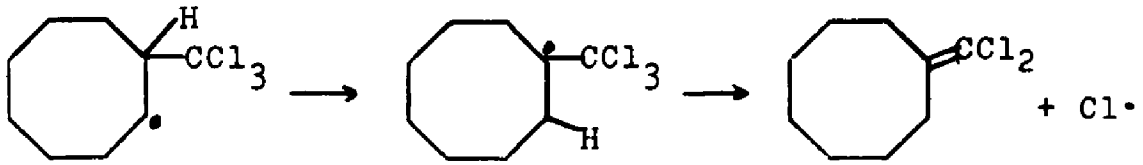


The formation of dichloromethylenecyclooctane is quite surprising. One can visualize at least two possible routes for its formation:

(1) dehydrochlorination of trichloromethylcyclooctane



(2) rearrangement of the initial 2-trichloromethylcyclooctyl radical



In the addition of CCl_4 to cyclodecene, the corresponding dichloromethylenecyclodecane was formed in 63% yield along with minor amounts of a transannular dichlorocyclodecane and some chlorocyclodecenes. These data seem to indicate path (2), since the first formed radical apparently does not exist long enough to abstract chlorine from the addend (CCl_4) to give disubstituted products. The 1,2 hydrogen shift (path (2)) should be favored energetically due to the relief of strain at carbon 1 in going to a trigonal carbon. Also, one could postulate a stabilization of the 1-trichloromethylcyclooctyl radical by a type of

hyperconjugative resonance involving the chlorines on the trichloromethyl group; however, few data are available to support this suggestion.

The postulation of a 1,2 hydrogen shift without additional evidence is somewhat presumptuous, since unequivocal examples of 1,2 radical rearrangements appear to be restricted to aryl groups and halogen atoms.[7] Perhaps deuterium labeling of the olefin would establish the intramolecular nature of this hydrogen shift.

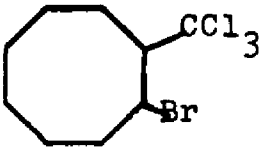
The other minor products in the CCl_4-cyclooctene reactions may be formed by hydrogen abstraction reactions occurring either before or after addition to cyclooctene. The variety of products formed illustrates the many possible reaction paths for these highly reactive intermediates.

B. Bromotrichloromethane Additions

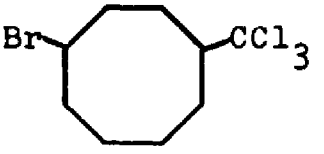
The abstraction of bromine from bromotrichloromethane occurs 150-2500 times faster than the abstraction of chlorine from carbon tetrachloride.[19] Thus, the intermediate 2-trichloromethylcyclooctyl radical formed by addition of bromotrichloromethane to cyclooctene will be more easily "trapped" before rearrangement to the 4-trichloromethylcyclooctyl radical. The principal addition product obtained from these additions was 1-bromo-2-trichloromethylcyclooctane. The structure was established by n.m.r. spectroscopy which revealed an A:B:C ratio of 8:4:2. The

TABLE III

PRODUCT DISTRIBUTION DATA FOR $BrCCl_3$ ADDITIONS TO CIS-CYCLOOCTENE



11



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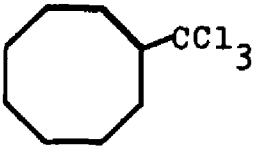

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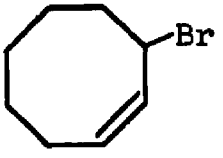

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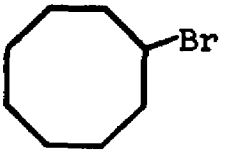


15

Others Unidentified

16

	Yield, Mole %					
Conditions[a]	11[b]	12[c]	13	14	15	16[d]
1.1 Moles cyclooctene 1.0 Mole $BrCCl_3$	22	2	38	30	3	1.0
1.0 Mole cyclooctene 4.0 Moles $BrCCl_3$	44	1.5	24	21	2	1.0

[a]See Experimental for details. [b]Both cis and trans isomers were obtained. [c]Calculated from the n.m.r. spectrum of 11; not isolated. [d]These figures exclude polymer and undistillable material.

existence of the 1,4 isomer(s) was inferred from the n.m.r. spectrum of the $C_9H_{14}Cl_3Br$ products obtained with excess cyclooctene in the addition reaction. The n.m.r. spectrum included a broad, weak signal centered at -4.23 p.p.m., ascribable to an isolated H-C-Br, and amounting to 10% of the total H-C-Br signal. Since the elemental analysis of this fraction is consistent with $C_9H_{14}Cl_3Br$, one may assume that this absorption is due to an isomer of the principal addition product. The A:B:C ratio of the product mixture is consistent with the assumption of 90% 1,2 and 10% 1,4 isomer distribution.

The proportion of this minor isomer decreased markedly when the addition was carried out in a large excess of $BrCCl_3$.

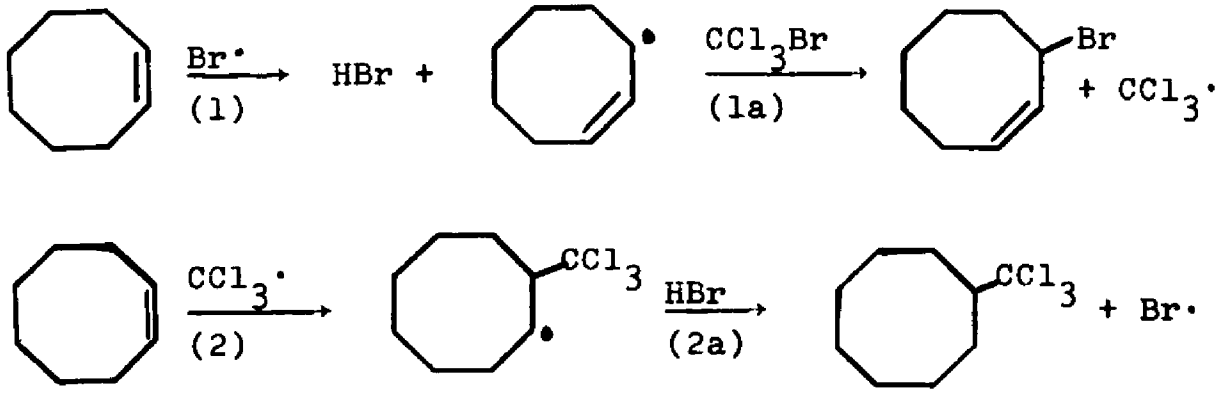
This change is understandable, since the rearrangement is intramolecular, while the addition requires a stepwise intermolecular mechanism. That is, excess $BrCCl_3$ favors the intermolecular, "trapping" reaction but does not affect the intramolecular rearrangement.

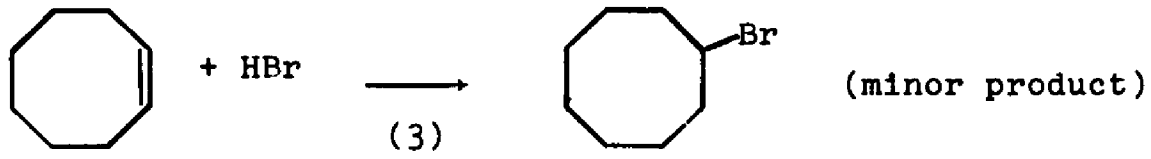
Allylic attack is of major importance in this addition; trichloromethylcyclooctane and 3-bromocyclooctene are the major products when the reaction is run at high olefin:addend ratios. The fact that they are formed in roughly equal yields (see Table III) suggests that they are formed concurrently by a rapid chain process. The details of the

chain mechanism must explain the relatively low yields of the corresponding compounds from the carbon tetrachloride additions.

Abstraction of the allylic hydrogen solely by the intermediate 2- or 4-trichloromethylcyclooctyl radicals would account for the relative amounts of these two products but not for the fact that less trichloromethylcyclooctane is formed in the CCl_4 additions, even though the intermediate trichloromethylcyclooctyl radicals presumably have a longer lifetime in the latter case.

A more reasonable mechanism would require a free bromine atom to abstract the allylic hydrogen of cyclooctene to form hydrogen bromide, which could transfer hydrogen to either the 2- or 4-trichloromethylcyclooctyl radicals to give the observed trichloromethylcyclooctane. The bromine atom thus formed could continue the chain. The details of the individual steps are summarized by the equations below:





The difference between the yields of these products and the corresponding products from the carbon tetrachloride additions can now be rationalized by consideration of the energy requirements of steps (1a) and (2a). The relatively stabilized allylic radical cannot abstract chlorine from carbon tetrachloride in an exothermic step; thus the activation energy for chlorine abstraction in a step corresponding to (1a) is prohibitively high.[7,13] In contrast, the corresponding bromine abstraction from $BrCCl_3$ is exothermic and rapid.[7,13,20]

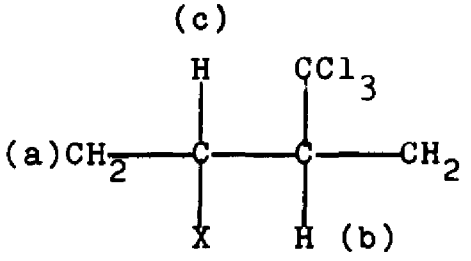
Hydrogen abstraction by a carbon radical (2a) is endothermic for abstraction from hydrogen chloride (by about 5 Kcal./mole), but is exothermic for abstraction from hydrogen bromide.[7,13] Thus, the slow rates of (1a) and (2a) for carbon tetrachloride prohibit any extensive contribution by this mechanism. The formation of cyclooctyl bromide is evidence for the presence of hydrogen bromide as an intermediate product.

When excess $BrCCl_3$ was used, the proportion of the reaction that proceeded by this path decreased from 70 to 45%, suggesting a higher kinetic order in cyclooctene for

the allylic abstraction reaction than for the addition reaction. That is, as the mole fraction of cyclooctene is decreased, the proportion of allylic abstraction decreases with respect to the proportion of addition reaction.

N.m.r. Spectra of 1-Bromo-2-trichloromethylcyclooctane and 1-Chloro-2-trichloromethylcyclooctane

The n.m.r. spectra of the above products are quite similar. A curious feature of both spectra is the signals for H-C-Br(Cl) which appeared as two triplets separated by 16 and 18 c.p.s., respectively.



X = Cl or Br

This multiplicity is what would be expected for the (c) signal if it were split into a doublet by proton (b) and into a triplet by the (a) protons. However, the coupling between b and c (16 c.p.s.) would have to be much larger than any vicinal coupling constant heretofore measured.[21] Also, the spacing in each triplet is not identical, indicating that they can not be components of the original doublet.

When the spectrum of the bromo-compound was run at 100 megacycles,[22] the apparent splitting increased to 27 c.p.s. Also, the complex signal due to H-C-CCl_3 split into two signals. Since coupling constants are independent of field strength,[21] these data prove conclusively that the two triplets (about 0.5 proton each) are due to two different chemical species. The A:B:C ratio indicates that the mixture contains only the 1,2 isomer(s). Therefore, two explanations are possible: (1) the mixture contains both the cis- and trans-1,2 isomers in approximately equal proportions, or (2) a single isomer exists in two conformations (equally significant at 35°) which interconvert very slowly with respect to the n.m.r. measurement.

The first explanation seems a priori the more appealing, since examples of fixed conformers at room temperature (35°) are rare. However, other data suggest that (2) cannot be eliminated. The sample sent for the 100 megacycle scan had a very sharp (1°) boiling point range. No separation of these isomers (presumably cis- and trans-1,2) is observed by gas chromatography. The same behavior is noted for the corresponding chloro-compound.

Additional experiments should be run to decide between these alternatives.* Separation into two products (however

---

*Very recent data pertaining to the solvent effect on the H-C-Br and H-C-CCl_3 proton spectra and 60 m.c. decoupling experiments prove the sample here is a cis-trans mixture. See Experimental (p. 63). These data were obtained Dec. 9, 1965.

incomplete) by some physical method such as liquid-solid chromatography would prove the cis-trans isomerism (1). On the other hand, if the H-C-Br signal tends to merge into a single peak at higher temperatures, only a single isomer in two conformations is present (2).

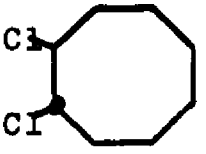
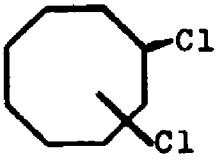
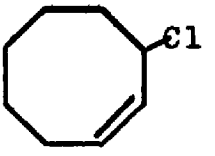
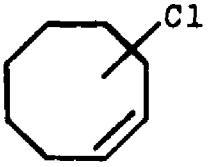
C. Chlorinations of Cyclooctene and Cyclodecene

Chlorinations of olefins by either an ionic or free radical mechanism occurs at a very rapid rate.[14b] In the discussion of the mechanism of free radical chlorination (see Introduction) it was pointed out that the initiation step is rate determining and is second order in olefin. This description implies that the chain transfer step is faster than the initiation step and therefore probably much faster than transannular rearrangement. Accordingly, no transannular products were found in the chlorinations of cyclooctene and cyclodecene.

In the case of cyclooctene, the product distributions observed for the free radical and ionic chlorinations do not demand two different mechanisms. An important criterion for a purely ionic chlorination is the absence of any hydrogen abstraction products other than the allylic chloride, which can be formed by either mechanism.[14b] The results for cyclooctene indicate that the free radical path is important even when the solution is saturated with air. An alternative explanation for the presence of the chlorocyclooctene

TABLE IV

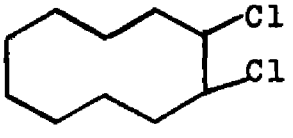
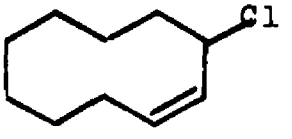
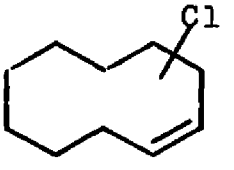
PRODUCT DISTRIBUTION DATA FOR CHLORINATION OF CIS-CYCLOOCTENE

Conditions[b]	Yield,[a] Mole %			
				
Free Radical Conditions	84	5	7	4
Ionic Conditions	88	2	5.5	4.5

[a]Yields were determined by gas chromatography. [b]See Experimental for details.

TABLE V

PRODUCT DISTRIBUTION DATA FOR CHLORINATION OF CIS-CYCLOOCTENE

Conditions[b]	Yield,[a] Mole %		
			
Free Radical Conditions	85	5	5[c]
Ionic Conditions	93	5	0

[a]Yields were determined by gas chromatography. [b]See Experimental for details. [c]Several products which were not resolved by gas chromatography.

(different from 3-chlorocyclooctene) in the ionic chlorination would be an ionic hydride shift to give the remote chlorocyclooctene. This explanation seems unlikely in view of the fact that no transannular dichlorides were observed.

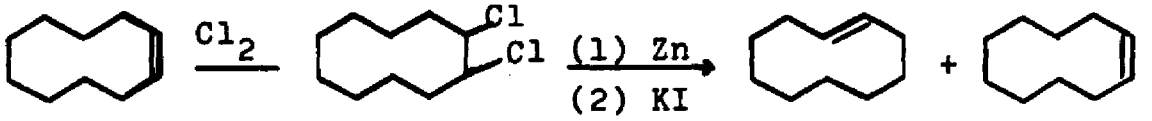
In contrast, ionic chlorination of cis-cyclodecene gave only one chlorocyclodecene. presumably 3-chlorocyclodecene, while the free radical chlorination gave a mixture (poorly resolved by capillary gas chromatography) of several chlorocyclodecenes.

For cyclodecene the ionic chlorinations were carried out using 100% oxygen; however, with cyclooctene, air was used to inhibit the radical reaction. This fact may be responsible for the differences noted.

The major product from the cyclooctene reaction was the previously reported[23a,b,c] trans-1,2-dichlorocyclooctane, while a minor amount (5% and 2% for the free radical and ionic chlorinations, respectively) of a second isomer was observed by gas chromatography. This minor isomer is probably cis-1,2-dichlorocyclooctane, since the mixture was converted almost quantitatively to cis-cyclooctene by treatment with zinc dust. The cis-1,2-dichlorocyclooctane would give the unstable trans olefin which would be expected to isomerize to the cis olefin over zinc chloride at 135°.

The $C_{10}H_{18}Cl_2$ product obtained from either ionic or free radical chlorination of cis-cyclodecene was homogeneous

to gas chromatography at several temperatures on two columns. Also, elution chromatography on alumina yielded 15 fractions with identical infrared spectra. Treatment with zinc dust at 135°(see Experimental) led to a mixture of 61% trans- and 39% cis-cyclodecene. Treatment with potassium iodide in Cellosolve (ethylene glycol monoethyl ether) led to a mixture of 75% trans- and 25% cis-cyclodecene.



(1) 61% 39%
(2) 75% 25%

The predominant formation of trans-cyclodecene from both dechlorination reactions indicated that either (1) both potassium iodide and zinc reactions involved cis elimination from the trans dichloride, or (2) that the initial adduct was cis-1,2-dichlorocyclodecane and trans elimination of chlorine was involved. The possibility of isomerization of the olefin cannot be overlooked; however, the equilibrium would favor the formation of the more stable cis-cyclodecene.

The available data suggest that the initial dichlorocyclodecane is predominantly the cis isomer, since the elimination reactions have been shown to occur by a trans mechanism.[24] Also, the complex nature of the H-C-Cl signal for this compound suggests the cis isomer. The trans isomer would favor equivalent protons (H-C-Cl) in any conformation.

The cis isomer contains in each conformation nonequivalent protons which become equivalent by conformational equilibrium. If the two protons are nonequivalent for a time interval which is long compared to the n.m.r. measurement, the protons will couple and split each signal into a doublet. Accordingly, authentic trans-1,2-dichlorocyclooctane gave a narrow band of four peaks with a low intensity absorption on either side of the major absorption. The H-C-Cl spectrum of the 1,2-dichlorocyclodecane obtained in this work revealed twelve peaks under high resolution: eight major peaks and a pair of low intensity absorptions on each side of the main band. The signal was somewhat broader than for trans-1,2-dichlorocyclooctane.

If either cis- or trans-1,2-dichlorocyclodecane (previously undescribed) could be synthesized by stereochemically reliable methods, this question would be resolved.

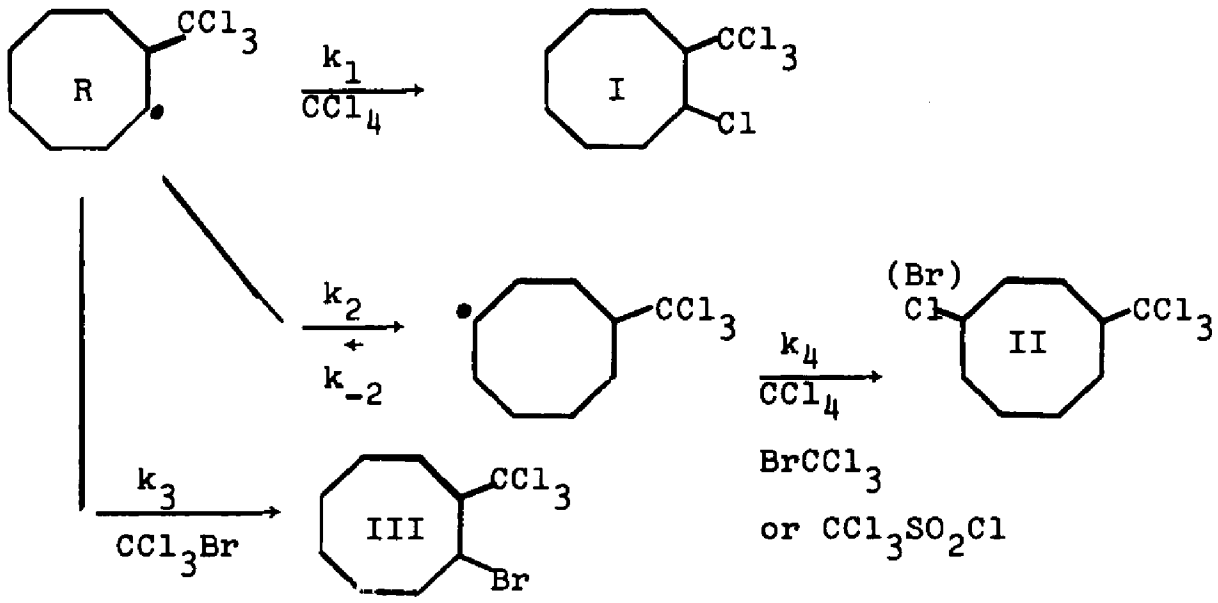
D. Kinetic and Energy Considerations

The competition between transannular and vicinal addition depends on the nature of the addend, the temperature and the concentration of the olefin and addend species. The intermediate 2-substituted-cyclooctyl radical is "trapped" by good transfer agents such as chlorine and bromotrichloromethane, while its reaction with carbon tetrachloride is sufficiently slow to allow transannular rearrangement. Trichloromethanesulfonyl chloride gives

substantial yields of both types of addition products and represents an intermediate case.

The ratio of transannular to vicinal products was 20:1 for CCl_4 addition and 1:30 for $BrCCl_3$ addition for the experiments in which the addend to olefin ratio was 4:1. Thus, the ratio of rate constants for bromine abstraction to chlorine abstraction in this work was 600:1. The relative rate constants for transannular migration vs addition cannot be compared by such a simple procedure since they follow a different kinetic order and depend markedly on the addend to olefin ratio.

If we assume that the 2-trichloromethylcyclooctyl radical is formed in a kinetically fast step, the alternative reactions of this intermediate may be summarized by the following scheme:



This scheme may be simplified if one makes the assumption that k_{-2} is very small and unimportant in the overall kinetic scheme. This should be a very good approximation since the rearranged radical should be more stable than the initial radical by at least 4 Kcal./mole (see Introduction). Thus, the activation energy for the process associated with k_{-2} is larger than that for the process associated with k_2 by an amount equal to the heat of reaction for the rearrangement and should be quite large.[25] With this assumption, one may conclude that the process associated with k_4 is faster than the process associated with k_{-2} and need not be considered as a rate determining step. If the various products are labeled as R, I, II, and III, as in the diagram above, we have:

$$dI/dt = k_1[R]\cdot[CCl_4] \qquad dII/dt = k_2\cdot[R]$$

$$dIII/dt = k_3\cdot[R]\cdot[CCl_3Br]$$

If one assumes the ratio of products is constant throughout the reaction or that the reaction is carried out to small conversions, the dependence on time and radical concentration may be removed by studying the <u>ratio</u> of products.

$$\frac{I}{III} = \frac{k_1}{k_3} \cdot \frac{[CCl_4]}{[CCl_3Br]} \qquad \frac{I}{II} = \frac{k_1 \cdot [CCl_4]}{k_2}$$

$$\frac{III}{II} = \frac{k_3 \cdot [CCl_3Br]}{k_2}$$

If one considers the I/III ratio (1/600 with excess addend) k_1 and k_3 may be compared directly giving $k_3 = 600\ k_1$. The difference in the free energies of activation for the steps may be calculated as follows:

$$\frac{I}{III} = 1/600 = \exp(-\Delta F_1^*/RT) \cdot/\cdot \exp(-\Delta F_3^*/RT)$$

$$-\ln 600 = -(\Delta F_1^* - \Delta F_3^*)/RT; \quad \begin{matrix} T = 317^\circ K \\ RT = 0.634 \text{ Kcal./mole} \end{matrix}$$

$$3.5 \text{ Kcal./mole} = \Delta F_1^* - \Delta F_3^*$$

$$= \Delta H_1^* - \Delta H_3^* - T(\Delta S_1^* - \Delta S_3^*)$$

The entropies of activation for the two processes should be quite similar except for the difference in the symmetry numbers of CCl_4 (12) and $BrCCl_3$ (3). This takes into account the fact that 4 chlorines are available for abstraction from CCl_4 but only one bromine from CCl_3Br. Thus,

$$\Delta S_1^* - \Delta S_3^* = R\ln 12/3 = 1.38\ R \text{ e.u.}$$

$$-T\ (1.38\ R) = -0.87 \text{ Kcal./mole}$$

$$\Delta H_1^* - \Delta H_3^* = 4.4 \text{ Kcal./mole}$$

In spite of the crude nature of these calculations, similar results are obtained for the difference in the activation energies for chlorine and bromine abstraction calculated from the transfer constants in styrene and methyl acrylate polymerizations.[26]

	Styrene	Addend	Methyl Acrylate
E^*	12.3 Kcal./mole	CCl_4	13.3 Kcal./mole
E^*	9.0	CBr_4	7.7
ΔE^*	3.3		5.6

Hirschfelder predicts on theoretical grounds that the activation energy for a series of similar radical abstraction reactions should be proportional to the bond dissociation energy of the bond being broken.[27] This rule applies only to exothermic reactions. The bond dissociation energies of CCl_3-Cl, CCl_3-Br, and CBr_3-Br are 68, 49, and 49 Kcal./mole, respectively.[28] For polyhalomethanes, it appears that the activation energy amounts to 18% of the bond dissociation energy. The activation energy for chlorine abstraction from CCl_4 by the 2-trichloromethylcyclooctyl radical should be in the range of 11-14 Kcal./mole and that for bromine abstraction should be in the range of 7-9.5 Kcal./mole.

The product distribution data indicate that the rate of transannular hydrogen atom abstraction lies intermediate between chlorine abstraction and bromine abstraction.

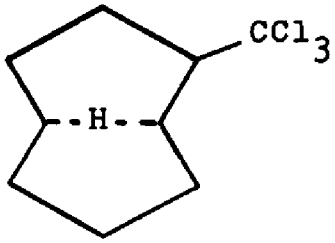
However, it is very unlikely the activation energy (enthalpy) for this process is intermediate to the values estimated for the halogen abstraction processes.

The carbon-hydrogen bond being broken has a bond dissociation energy of approximately 94 Kcal./mole.[29] If one makes the assumption that the activation energy for breaking this bond amounts to 18% of the bond dissociation energy (as for the halogen abstraction processes), application of Hirschfelder's rule would predict an activation energy of 17 Kcal./mole. Calculations by Johnson and Parr[30] predict an activation energy of 12 Kcal./mole for the hydrogen transfer reaction between a secondary hydrogen on propane and an isopropyl radical. These authors,[30] however, point out that the model used for this calculation ignores non-bonded interactions and that the predictions are several Kcal./mole too low for sterically hindered systems. This model probably over-emphasizes the strength of the bond being formed, while Hirschfelder's model ignores this factor as long as the overall transfer is exothermic.

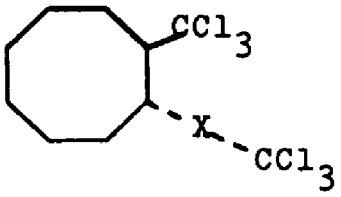
The values of 12 and 17 Kcal./mole probably represent limits for the activation energy of the transannular hydrogen atom transfer. The important point here is that the activation energy for this process is probably higher than that for chlorine abstraction from CCl_4.

The rearrangement is unimolecular and would, therefore, have a very different entropy of activation compared to the

bimolecular abstraction. The origin of this entropy difference is apparent if we examine the probable structure for the transition states for the formation of I, II, and III.



Transition State
for II



X = Br,Cl

Transition State
for I or III

In the transition state for I and III, the translational entropy of one mole of CCl_3-X has been lost in going from the "ground" state (R and CCl_3-X separated) to the transition state. The magnitude of this entropy change is difficult to calculate for the liquid state; however, it should be in the range of -20 to -35 e.u. This estimate is based on the reported entropy of activation (ΔS^{*} = -32 e.u.) for the dimerization of cyclopentadiene, in which the translational entropy of one mole of reactant is lost in the transition state.[31] Other entropy effects, such as the loss of vibrational degrees of freedom in the transition state for II compared to I and III, could be considered. These effects would be small compared to the translational entropy and would probably allow one to lower the estimated differences in entropies of activation by several e.u.

The effect of this entropy difference would be an acceleration of the transannular migration compared to the normal addition by a factor of 10^3 to 10^6. Thus, the energy of activation for the transannular migration could easily be 4 to 7 Kcal./mole larger than that for chlorine abstraction and still compete favorably due to the compensating entropy effect. The proportion of 1,2 addition product from CCl_4 at 150° (1.2%) is smaller than that at 44° (3.8-5%), indicating that the transannular migration has a larger activation energy.*

The considerations presented here by no means constitute a calculation of the kinetic parameters involved. The reactions were, in general, run to high conversion and the analytical techniques for determination of the proportion of the minor isomers were subject to large percentage errors. Qualitatively, the competition between transannular and normal addition depended principally on the strength of the bond being broken in the addend molecule, with secondary effects due to concentration and temperature. The transannular process would be favored at high temperatures and high olefin-to-addend ratios.

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*Higher temperatures would favor the reaction with the higher activation energy by a factor of $\exp((\Delta\Delta H^{\ddagger}/R)\cdot(T_2-T_1)/T_1T_2)$; $\Delta\Delta H^{\ddagger}$ and (T_2-T_1) are positive.

CHAPTER III

EXPERIMENTAL

Elemental analyses were performed by Mr. R. Seab of these laboratories and are given as the average of three determinations.* Gas chromatographic analyses were obtained with a Barber Coleman Model 20 instrument equipped with a hydrogen flame detector and a 100 foot capillary column coated with GE-96 silicone. Preparative gas chromatography was performed on a Wilkens Aerograph Autoprep Model A-700 instrument equipped with a 3/8 inch x 20 foot silicone column. N.m.r. spectra were run by R. Seab or W. Wegner on a Varian Associates HA-60 spectrometer with tetramethylsilane internal reference. The 100 megacycle n.m.r. spectrum was run by R. Pitcher of Varian Associates, Houston, Texas. I.R. spectra were obtained with Beckman IR-5 and IR-7, and Perkin-Elmer Model 21 and 137 instruments. Capillary melting points were obtained with a Thomas-Hoover apparatus and are uncorrected. Photo-initiated reactions were carried out in a Rayonet Photochemical Reactor utilizing 16 lamps of either 2537 Å or 3500 Å light.

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*For hydrogen analyses the average deviation from the average was 0.03% and in no case did a single determination differ from the average by more than 0.11%. For carbon the average deviation was 0.07% and the greatest deviation was 0.20%.

A. Photo-initiated Addition of Carbon Tetrachloride to cis- Cyclooctene

A solution of freshly distilled cis-cyclooctene[32] (75 g., 0.68 mole) in reagent grade carbon tetrachloride (600 g., 2.64 moles) was placed in a 500 ml. quartz flask and deoxygenated by a nitrogen stream for 10 minutes. The flask was lowered into a Rayonet Photochemical Reactor and irradiated with 2537 Å light while a nitrogen atmosphere was maintained over the reaction mixture. A cooling fan kept the reaction mixture at 44°. After 20 hours of illumination, a dark film of polymeric material coated the sides of the flask, and illumination was interrupted while the reaction vessel was cleaned. The mixture was returned to the flask, swept with nitrogen for 5 minutes and illumination was continued for an additional 20 hours.

The excess CCl_4 was removed from the mixture by rotary evaporation, and the residue (200 g.) was distilled at reduced pressure to give the following fractions:

I	14 g.	Dry Ice trap (density approximately 1.07, corresponding to 8 g. cyclooctene (d_{20}^{20} = 0.85) and 6 g. CCl_4 (d_4^{20} = 1.59)).
II	1.5 g.	b.p. 45-70° (0.2 mm.)
III	12 g.	b.p. 70-97° (0.2 mm.)
IV	129 g.	b.p. 97-116° (0.2 mm.)
V	residue	approximately 15 g.

1. Identification of Major Fraction IV

Fraction IV was redistilled to give 124 g. of a product whose analysis indicated a 1:1 addition product.

Anal. Calc. for $C_9H_{14}Cl_4$: C, 40.90; H, 5.34. Found: C, 41.15; H, 5.75.

The yield based on cyclooctene consumed (67 g.) was 72%.

A portion of this mixture (4.5 g.) was reserved for infrared analysis while the remainder (119.5 g.) was dissolved in twice its volume of absolute methanol and chilled to -60° in a Dry Ice-acetone bath. The solid material which separated was filtered and recrystallized three times from absolute methanol (-10 to -30°), yielding 35 g. of a white crystalline material (m.p. 64-65.5°), IV(s).

Anal. Calc. for $C_9H_{14}Cl_4$: C, 40.90; H, 5.34. Found: C, 41.07; H, 5.78.

The methanol solutions from the above crystallizations were combined, concentrated to about one half of their original volume and cooled to -60°, yielding 5 grams more of crystalline material. The combined liquid phases were distilled, yielding 70 g. of a liquid (b.p. 127-130° @ 2 mm.), IV(l).

Anal. Calc. for $C_9H_{14}Cl_4$: C, 40.90; H, 5.34. Found: C, 41.02; H, 5.58.

A gas chromatogram of IV(l) showed the presence of a third isomer (3.8% yield) which is a major product in the CCl_3SO_2Cl-cyclooctene reaction (described later).

2. Infrared Spectra of IV(s) and IV(l); Analysis of Mixture IV

Both compounds give intense absorption for the trichloromethyl group in the region of 12.8-13.5 μ. No evidence for vinyl hydrogen or unsaturation was observed. The C-Cl stretching frequency is 14.9 μ for IV(s) and 14.81 μ for IV(l). The two isomers give quite similar spectra in the 7-11 μ region except for the relative intensities of the peaks. Two peaks, 10.2 μ and 10.5 μ, were chosen for analysis of the mixture. Standard solutions of each isomer and the mixture IV were prepared by dissolving 4.445 g. of each in CS_2 and diluting to 50 ml. in a volumetric flask. Standard mixtures of IV(s) and IV(l) were prepared gravimetrically from these solutions. The absorbances at 10.2 and 10.5 μ were determined in a 0.5 mm. cell on the Perkin-Elmer 21 instrument. The ratio of absorbance at 10.2 μ to that at 10.5 μ ($A_{10.2}:A_{10.5}$) vs mole fraction IV(l) was plotted over the entire range of concentrations, giving a smooth curve.

Mole fraction IV(l)	$A_{10.2}:A_{10.5}$
0.0	0.85
0.25	1.34
0.50	1.88
0.61	2.18
0.66	2.35
1.00	3.15

The value of $A_{10.2}:A_{10.5}$ for the initial mixture was 2.22, which corresponds to 64% liquid isomer. This is in

excellent agreement with the observed ratio of separated isomers, 70:40 (64% liquid isomer).

3. N.m.r. Spectra of IV(s) and IV(l)

The n.m.r. spectrum of IV(l) showed the following absorptions: -4.23 p.p.m. (1 proton, Cl-C-H), -2.6 p.p.m. (1 proton, CCl_3-C-H), -2.2 p.p.m. (7.5 protons, CH_2-C-X; X = Cl, CCl_3), and -1.65 p.p.m. (4.5 protons, CH_2-CH_2-CH_2). The assignment of the absorption at -1.65 p.p.m. is consistent with the n.m.r. spectrum of cyclooctane, which gives a single peak at -1.65 p.p.m.

The n.m.r. spectrum of IV(s) showed absorptions at -4.20 p.p.m. (1 proton, H-C-Cl), -2.75 p.p.m. (1 proton, CCl_3-C-H), a complex group of absorptions from -2.6 to -1.8 p.p.m. (8 protons, CH_2-C-X; X = Cl, CCl_3) and -1.65 p.p.m. (4 protons, CH_2-CH_2-CH_2). The n.m.r. spectra of both of these compounds exclude 1,2 addition products which would be expected to give an eight proton absorption peak at -1.65 p.p.m.

B. Basic Dehydrochlorination of IV(s) and IV(l)

1. IV(s). To a solution of 4 g. (0.015 mole) of the solid isomer in 20 ml. of dimethyl sulfoxide (DMSO) was added a solution of 1.0 g. of potassium hydroxide (0.016 mole) in 5 ml. of 50% ethyl alcohol and 25 ml. of DMSO. The mixture was stirred for 4 hours at room temperature and finally poured into 75 ml. of water. The water solution was

extracted twice with 50 ml. portions of petroleum ether. The petroleum ether solution was washed 3 times with water, dried over $CaSO_4$, and concentrated by rotary evaporation. Gas chromatographic analysis showed 86% conversion of the starting material to olefinic products, shown by gas chromatography to be 92% of one product (b.p. 115-117° @ 1.8 mm.).

2. IV(1). Identical treatment of IV(1) (5 g., 0.019 mole) with 1.23 g. (0.019 mole) of potassium hydroxide led to 75% conversion of the starting material to olefinic products of which 88% was a product having an identical gas chromatographic retention time and infrared spectrum as the product obtained from IV(s).

Dehydrochlorination in aqueous ethanol or methanol gave low conversions, even after extended reaction at refluxing temperatures. The use of potassium t-butoxide in anhydrous DMSO gave a very rapid, exothermic reaction but the yield of the above product was 15-20%. In both of the above cases, complex mixtures of products were obtained.

3. Dehydrochlorination of the Mixture IV. In a preparative scale run, 50 g. (0.19 mole) of the mixture IV was dissolved in a mixed solvent (120 ml. of DMSO, 5 ml. of H_2O, 35 ml. of MeOH). To this solution was added dropwise a solution of 14 g. of KOH (82%, 0.20 mole) in a solvent containing 10 ml. of H_2O, 25 ml. of DMSO, and 25 ml. of MeOH.

The reaction flask was maintained at room temperature (28°) by means of a surrounding water bath. After five hours of stirring, 50 ml. of MeOH was added to obtain a homogeneous solution. The mixture was stirred for three additional hours, then poured into 300 ml. of water. The water solution was extracted with four 150 ml. portions of petroleum ether. The combined organic solutions were reduced to 400 ml. by evaporation and finally washed three times with 250 ml. portions of water. After removal of the solvent by rotary evaporation, gas chromatography showed 82% product, 9% unreacted $C_9H_{14}Cl_4$, and 9% other products. Distillation afforded 30 g. (b.p. 121-123° @ 3.5 mm.) in the center cut (70%).

Anal. Calc. for $C_9H_{13}Cl_3$: C, 47.55; H, 5.76. Found: C, 47.53; H, 5.73.

The infrared spectrum was devoid of vinyl hydrogen absorption (3.3 μ) but showed intense bands at 6.23 μ and 11.1 μ. These latter bands have been reported as characteristic of an exocyclic dichloromethylene grouping.[33] Also, no intense band was noted in the region of 13 μ, indicating that the $-CCl_3$ grouping was absent.

The n.m.r. spectrum also gave no evidence for vinyl hydrogen. A one proton absorption at -4.1 p.p.m. (due to H-C-Cl) was a quintet (J = 5.5 c.p.s.) indicating four nearly equivalent neighbors. The resolution of this multiplet was

poor at room temperature, but improved as the probe temperature was increased to 60°.

These data indicate that the dehydrohalogenation product is a dichloromethylenechlorocyclooctane and that IV(s) and IV(l) are geometrical rather than positional isomers.

4. Ozonation of the Dehydrohalogenation Product. A solution of 10 g. (0.044 mole) of the above dichloromethylenechlorocyclooctane in 50 ml. of CCl_4 was treated with a stream of 5% ozone[34] at 0°. After 0.052 mole of ozone had been introduced (5 hours), the saturated solution was allowed to stand several hours at 0°. The CCl_4 solution was transferred to a 250 ml. round bottom flask which was placed on a rotary evaporator to remove the CCl_4. Care was taken not to heat the flask above 45°. The residue, a gummy semi-solid, was dissolved in 100 ml. of glacial acetic acid. The acetic acid solution of the ozonide was cooled by a surrounding water bath and was stirred vigorously during the addition of 6.5 g. of powdered zinc. After the addition of the zinc (45 minutes), the cooling bath was removed, and the mixture was stirred for an additional hour and then poured into 200 ml. of water. This solution was extracted three times with petroleum ether. The combined petroleum ether fractions were extracted twice with water and once with 5% $NaHCO_3$. After drying over $MgSO_4$ and removal of the

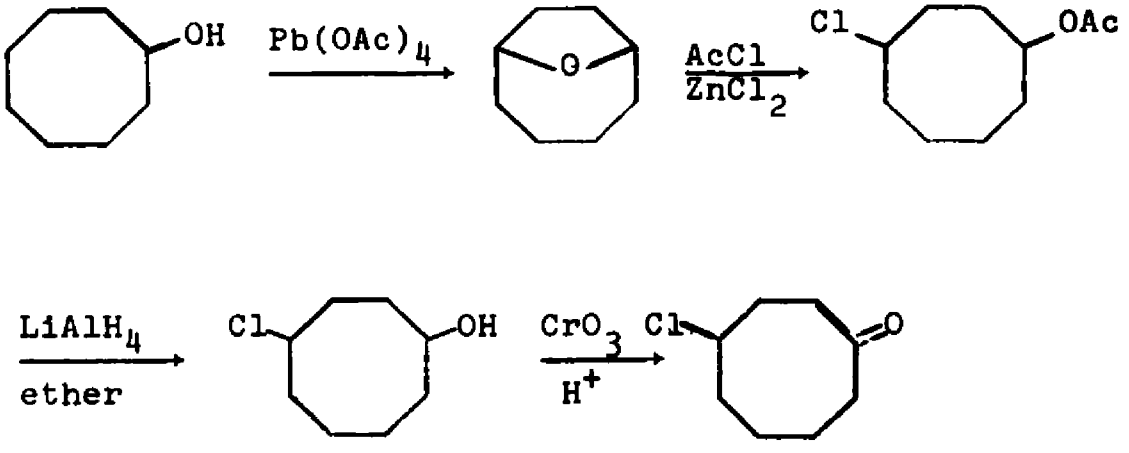
solvent, a sample of the residue (6 g.) was injected into the gas chromatograph. The following peaks and relative areas were recorded: chlorocyclooctanone, 50%; recovered starting material, 30%; a cyclooctenone,[35] 12%; and other unidentified products, 8%.

The chlorocyclooctanone exhibited intense infrared absorption at 1706 $cm.^{-1}$, excluding 2-chlorocyclooctanone (C = O absorptions at 1714 and 1725 $cm.^{-1}$).[36]

The 2,4-dinitrophenylhydrazone of this ketone was initially an oil which crystallized from 95% ethanol. After three recrystallizations from 95% ethanol, the derivative melted at 150-152°.

Anal. Calc. for $C_{14}H_{17}N_4O_4Cl$: C, 49.35; H, 5.45. Found: C, 49.42; H, 5.54.

This product was shown to be 4-chlorocyclooctanone by the following independent synthesis.



C. Synthesis of Authentic 4-Chlorocyclooctanone

1. 9-Oxabicyclo[4.2.1]nonane[37]

A mixture of 125 g. (0.282 mole) of $Pb(OAc)_4$ and 35 g. (0.35 mole) of $CaCO_3$ in 400 ml. of dry benzene was refluxed for 30 minutes. To this refluxing solution was then added dropwise a solution of 38.4 g. (0.30 mole) of cyclooctanol in benzene. The mixture was refluxed for 14 hours, allowed to cool and filtered. The solid was washed with 100 ml. of petroleum ether, and the combined organic fractions were washed with water and dried over $CaCl_2$. The solvent was removed by rotary evaporation, and the residue was distilled through an 8 inch packed, heated column. The fraction collected at 105-110° (90 mm., 5 g.) had an infrared spectrum identical to the published[38] spectrum for 9-oxabicyclo[4.2.1]nonane and was apparently free of the [3.3.1] isomer. Gas chromatographic analysis showed 88% purity with benzene and cyclooctanone (4%) an impurities.

2. cis- and trans-4-Chlorocyclooctyl Acetate from 9-Oxabicyclo[4.2.1]nonane

The 9-oxabicyclo[4.2.1]nonane (2.6 g., 0.018 mole) was added to 15 g. of acetyl chloride in a 50 ml. round bottom flask equipped with a reflux condensor. A small amount of zinc chloride[39] (about 0.5 g.) was added, and the vigorous reaction which began immediately was moderated by cooling the reaction flask in a water bath. After the initial reaction had subsided, the mixture was refluxed for

20 minutes. Gas chromatographic analysis indicated that no 9-oxabicyclo[4.2.1]nonane remained in the mixture.[40] The mixture was diluted with 25 ml. petroleum ether, the excess acetyl chloride was hydrolyzed with ice, and the layers were separated. The aqueous phase was extracted with 50 ml. of petroleum ether and the combined petroleum ether phases were washed twice with water. The solution was dried over $MgSO_4$ and concentrated by rotary evaporation. The residue was distilled, giving two fractions:

I	50-80° @ 2 mm., about 1 g.
II	85-115° @ 2 mm., 2.5 g.

Fraction I gave infrared bands characteristic of a cyclooctenyl acetate.[41] Fraction II gave infrared bands consistent with the 4-chlorocyclooctyl acetate (5.78 μ, 8.1 μ, and 14.9 μ). Gas chromatographic analysis showed two peaks for fraction II with relative areas 70:30. Because a single chloro ketone was ultimately obtained from this mixture, the two peaks were assumed to be associated with the geometric isomers of 4-chlorocyclooctyl acetate.

3. 4-Chlorocyclooctanol from $LiAlH_4$ Reduction of 4-Chlorocyclooctyl Acetate

The product mixture from the above reaction (2.5 g., 0.012 mole) was dissolved in 15 ml. of anhydrous ethyl ether and transferred to a pressure regulating dropping funnel. Lithium aluminum hydride (0.35 g., 0.009 mole) was dissolved in 15 ml. of anhydrous ether in a 3 neck, 100 ml.

flask equipped with a magnetic stirrer and reflux condensor. The ether solution of the ester was added at a rate which kept the solvent refluxing gently. The solution was refluxed for twenty minutes after addition of the ester was complete. Excess hydride was decomposed by the slow addition of 80% ethyl alcohol. The mixture was poured into a flask containing 50 ml. of 5% sulfuric acid, then extracted twice with petroleum ether, and finally washed twice with water. The solvent was removed, and the residue of 4-chlorocyclooctanol was used directly in the next step.

4. 4-Chlorocyclooctanone from CrO_3 Oxidation of 4-Chlorocyclooctanol

A solution of the product from the previous reaction in 25 ml. of acetone was cooled to 0° by means of an ice bath. Chromic acid solution (1.5 g., 0.015 mole, CrO_3 in 9 ml. of 30% H_2SO_4) was added dropwise until the orange color persisted (5 ml. of the CrO_3 solution). The reaction mixture was poured into 50 ml. water, then extracted twice with petroleum ether. The organic layer was washed several times with water to remove the acetone and was dried over $CaCl_2$. After removal of solvent, gas chromatographic analysis showed the product to be 70% of a compound which had a gas chromatographic retention time identical with that of the ketone from the ozonation procedure. The infrared spectrum (C = O, 1706 $cm.^{-1}$) also corresponded to the spectrum of the ketone from the ozonation procedure. The

2,4-dinitrophenylhydrazone melted at 149-151.5° and, when added to the derivative from the ozonation procedure, did not depress the melting point. The infrared spectra of the two derivatives in CS_2 were run on the same chart paper and were superimposable. The n.m.r. spectrum of the impure ketone showed a poorly resolved quintet at -4.15 p.p.m., indicating that the CH_2-C<u>H</u>Cl-CH_2 grouping was present.

The chlorocyclooctanone from the ozonation is thus identified as 4-chlorocyclooctanone. This identity establishes the structure of the dehydrohalogenation product as 1-chloro-4-dichloromethylenecyclooctane and that of the major addition products (IV) as the isomeric 1-chloro-4-trichloromethylcyclooctanes.

D. <u>Dehydrochlorination of IV(s) and IV(l) with Silver Nitrate</u>

Although basic dehydrochlorination of the $C_9H_{14}Cl_4$ isomers gave mainly the exocyclic olefin, treatment with $AgNO_3$ gave only the endocyclic olefin.

1. <u>IV(s)</u>. A solution of 9.04 g. (0.0342 mole) of the solid isomer and 6.00 g. of $AgNO_3$ (0.0350 mole) in 50 ml. of 90% methanol was stirred for four hours at 45°. The precipitated silver chloride was removed by filtration, and the reaction mixture was dissolved in ethyl ether. After several washings with water, the solution was dried with $MgSO_4$ and concentrated by rotary evaporation. Treatment of the aqueous phases with saturated NaCl solution

gave several grams of silver chloride. The product mixture was distilled to give three fractions:

I	74-75°	@ 0.15 mm., 0.9 g.
II	75-80°	@ 0.15-.20 mm., 3.1 g.
III	105-107°	@ 0.2 mm., 4 g.

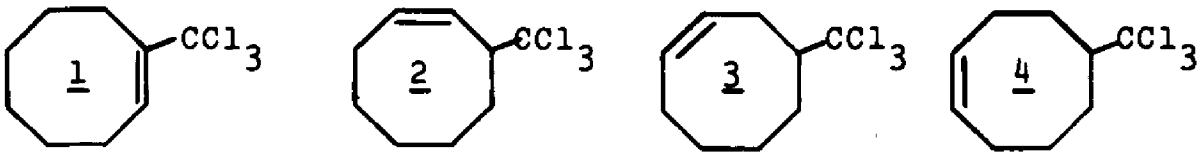
Fraction I gave only one major peak, corresponding to 97% purity, while fraction II contained this component in 99% purity. Fraction I contained a trace of a component (of lower retention time) giving an infrared absorption at 1737 $cm.^{-1}$ This peak did not belong to the major product, as indicated by its virtual absence in the spectrum of fraction II. The two fractions were otherwise identical. Fraction III crystallized in the distillation receiver and was identified as the starting material (m.p. 65°). The yield based on consumed $C_9H_{14}Cl_4$ was 93%. The conversion was only 55%, however, and was not increased substantially by prolonged heating.

Anal. Calc. for $C_9H_{13}Cl_3$: C, 47.41; H, 5.76. Found: C, 47.40; H, 5.93.

The infrared spectrum of this product indicated that it is one of the isomeric trichloromethylcyclooctenes. Bands were observed at 3.30 μ (vinyl hydrogen), 6.02 μ (C=C) and 12.8-13.6 μ (very intense, CCl_3). The n.m.r. spectrum showed two vinyl hydrogens at -5.7 p.p.m. with a splitting pattern almost identical to that reported for

cis-cyclooctene.[43] Other absorptions included a shoulder at -2.6 p.p.m. (about 1 proton, $\underline{H}$-C-CCl_3), -2.2 p.p.m. (6 protons, $C\underline{H}_2$-C-CCl_3 and $C\underline{H}_2$-C=C), and -1.6 p.p.m. (4 protons, CH_2-$C\underline{H}_2$-CH_2).

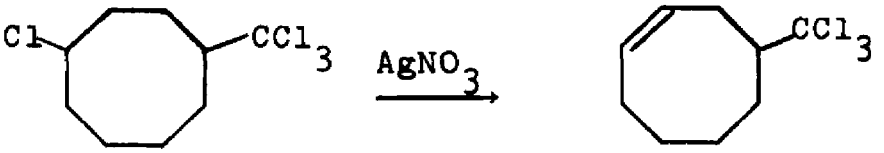
These data seem most consistent with the structure assignment of 4-trichloromethylcyclooctene (formula 3 below), rather than with any of the isomeric trichloromethyl-cyclooctenes.



A:B = 8:4 A:B = 6:4 A:B = 4:6 A:B = 2:8

Only 1 vinyl hydrogen would be observed for 1-trichlomethylcyclooctene, thus eliminating consideration of structure 1. Isomer 2 would have given two different signals for vinyl hydrogen and an A:B ratio of 6:4. Isomer 4 would have given an A:B ratio of 2:8. Only isomer 3 would be expected to give the observed 4:6 ratio.

The possibility that some 5-trichloromethylcyclooctene was also formed in this reaction cannot be eliminated. It is not uncommon for such isomers to have identical gas chromatographic retention times (as do 9-oxabicyclo[4.2.1]- and [3.3.1]nonanes)[43] and the experimental measurement of the A:B ratio is not sufficiently accurate to detect less than 4% of isomer 4.



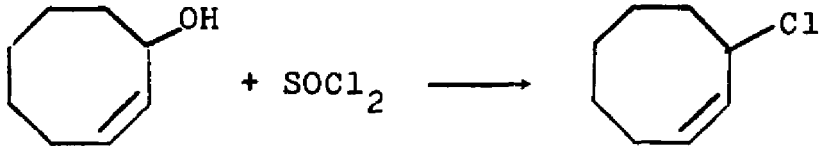
2. IV(1). Similar treatment of IV(1) (29.5 g., 0.115 mole) with silver nitrate (19.0 g., 0.116 mole) gave 12.8 g. (49.5% conversion) of a product which had an infrared spectrum and gas chromatographic retention time identical to those of the product obtained from the solid isomer, IV(s). The remainder of the reaction mixture was essentially unreacted IV(1).

E. Identification of Minor Products in CCl_4-Cyclooctene Addition Reaction

Although the $C_9H_{14}Cl_4$ products accounted for 72% of the product mixture, a low-boiling fraction (containing at least eleven products) was obtained in combined yields of 17%. The structures for seven of these products have been proposed (see table II), based on the available data. Careful distillation allowed separation of the product mixture into two fractions: (A) b.p. 45-60° @ 0.22 mm.; (B) b.p. 70-95° @ 0.22 mm. Fraction A comprised 2% of the total reaction mixture and contained four products. These products will be considered in the order of their gas chromatographic retention times and will be referred to as A-1, A-2, A-3, and A-4, respectively.

A-1 (0.07% yield) has the same retention time as hexachloroethane. In some of the runs, this material sublimed during distillation and formed several large crystals on the thermometer bulb. The infrared spectrum of this material was identical to the published[44] spectrum of C_2Cl_6, (sublimation temperature 184°, literature[44] 185°). Hexachloroethane was also prepared by extended photolysis of CCl_4 (under conditions similar to the reaction conditions) and was found to correspond to this material. The quoted yield of this product is probably low due to its volatility.

A-2 (0.75% yield) has the same retention time as 3-chlorocyclooctene. The authentic sample of this chloro olefin was prepared by treatment of 2-cyclooctene-1-ol with $SOCl_2$ (p. 77).[32]



When a small sample of the mixture A was treated with cold alcoholic silver nitrate an immediate precipitate formed, indicating the presence of an allylic chloride.

A-3 (0.61% yield) is formulated as chlorocyclooctane on the basis of its identical retention time with an authentic sample prepared by addition of HCl to cyclooctene (p. 76).[45]

A-4 (0.065% yield) No data are available for this compound which would allow structure assignment.

Fraction B contained at least seven products, comprising 13-15% of the entire reaction mixture. These products will be referred to as B-5 through B-11 in the order of their increasing retention times. Repeated distillation[46] of B (with combination of intermediate fractions) led to its separation into two groups: B-5, B-6, B-7, and B-8 comprising one group (containing two chlorines per eight or nine carbons) and B-9, B-10, and B-11 (containing three chlorines per cyclooctane group).

B-5 was formed in 0.8% yield. No data are available which would allow structure assignment.

B-6 (1.4% yield) had a gas chromatographic retention time identical with that of trans-1,2-dichlorocyclooctane. The preparation and characterization of an authentic sample will be described later in the discussion of the chlorination of cyclooctene (p. 78).

Preparative gas chromatography allowed isolation of B-7, B-9, and B-11 in purities of 91, 67, and 91%, respectively.

B-7 (2.8% yield) gave an elemental analysis that corresponded well with the assumption of two chlorines per nine carbon atoms: C, 55.26; H, 7.44. (For example, $C_9H_{14}Cl_2$ requires C, 56.0; H, 7.34). The infrared spectrum

showed only trace absorption for vinyl hydrogen, probably due to impurities, and intense absorption at 6.21 and 11.1 μ, due to $C{=}CCl_2$.[33] This compound is most probably dichloromethylenecyclooctane.

B-8 (1.8% yield) was not resolved from B-7 and B-9 on the preparative column but was collected in two fractions in 26% and 11% concentrations. The first fraction contained B-7 and B-9 in addition to B-8, while the second fraction contained B-9 and B-11. Carbon-hydrogen analyses were obtained for each fraction collected, and the relative amounts of each component were determined by capillary gas chromatography. If one assumes that only carbon, hydrogen and chlorine are present in these compounds, the percentage of chlorine may be obtained by the formula: %Cl = 100 - (%C + %H). By assuming B-7 = 37% chlorine (corresponding to $C_9H_{14}Cl_2$) and B-11 = 47% chlorine ($C_9H_{15}Cl_3$), solutions of two simultaneous equations gave B-8 = 39% chlorine and B-9 = 47% chlorine. These results imply that B-8 contains two chlorines per C_8 or C_9 group, while B-9 contains three chlorines per C_8 or C_9 group.

B-9 was collected in one fraction in 67% purity. The infrared spectrum of this fraction gave absorptions at 3.3 μ, 6.03 μ, and 13 μ (the latter was very intense, indicating a trichloromethyl grouping). These data indicate a trichloromethylcyclooctene as the structure. The gas

chromatographic retention time and infrared spectrum of this product differ from those of the trichloromethylcyclooctene derived from silver nitrate treatment of the 1-chloro-4-trichloromethylcyclooctane. This product is formulated as either 1- or 3-trichloromethylcyclooctene.

B-10 (0.22% yield) has a retention time between B-9 and B-11 (trichloromethylcyclooctane, described below) and probably contains three chlorines per C_8 or C_9 group.

B-11 (5.0% yield) was collected in 91% purity. The infrared spectrum showed no evidence of unsaturation and a very intense absorption at 13 μ ($-CCl_3$). The n.m.r. spectrum showed the following absorptions: -2.6 p.p.m. (1 proton, $\underline{H}-C-CCl_3$), -2.2 p.p.m. (4 protons, $C\underline{H}_2-C-CCl_3$), and -1.6 p.p.m. (8 protons, $CH_2-C\underline{H}_2-CH_2$).

Anal. Calc. for $C_9H_{15}Cl_3$: C, 47.20; H, 6.55. Found: C, 47.67; H, 6.90.

An authentic sample of trichloromethylcyclooctane was prepared by the photochemical reaction of chloroform with cyclooctene (described later, p. 74) and found to correspond to this material.

F. Thermally-initiated Addition of CCl_4 to Cyclooctene[47]

A mixture of cis-cyclooctene (61 g., 0.55 mole) and carbon tetrachloride (470 g., 3.1 mole) was heated in a Paar medium-pressure apparatus at 155° for 4.5 hours

(pressure reading was 100 lb./in.^{2}). After removal of excess carbon tetrachloride by rotary evaporation, reduced pressure distillation gave three fractions:

A 5.5 g., b.p. 30-70° @ 1.4 mm.
B 9.6 g., b.p. 70-108° @ 1.4 mm.
C 52 g., b.p. 108-130°@ 1.4 mm.

Fraction C was redistilled giving a mixture of $C_9H_{14}Cl_4$ isomers which corresponded to the fraction obtained from the photochemical run. Infrared analysis of this mixture (described previously) indicated 67% liquid isomer and 33% solid isomer. The two isomers were separated as before, giving a solid (m.p. 64-65.5°) and liquid fraction. The solid did not depress the melting point of the solid obtained in the photochemical experiment. A gas chromatogram of the liquid product indicated a 1.2% yield of a third isomer which was shown later to be the 1,2 addition product. Both liquid and solid isomers were again dehydrochlorinated with KOH in alcoholic DMSO to the same 1-chloro-4-dichloromethylenecyclooctane, reconfirming the geometrical isomerism of the two products.

Gas chromatographic analysis of the low-boiling fractions A and B indicated at least 14 minor products in combined yields of 24%. The yields of the various products are summarized in Table II. Two striking differences are noted in the distribution of these minor products; the high

yield of chlorocyclooctane in the thermal reaction (8.2 vs 0.61%) and the low yield of trichloromethylcyclooctane (0.30 vs 5.0%).

G. Photo-initiated Addition of CCl_4 to cis-Cyclooctene in Benzene Solvent*

The procedure used is the same as that previously described except for the addition of reagent grade benzene. A solution containing 26.8 g. (0.25 mole) of cyclooctene, 500 g. (3.2 moles) of carbon tetrachloride, and 100 g. benzene was irradiated with 2537 Å light in a quartz flask under a nitrogen atmosphere for 41 hours. After removal of solvent, the mixture was distilled at reduced pressure to give 43 g. of $C_9H_{14}Cl_4$ and 8 g. of low-boiling products.

The conversion of cyclooctene to products was 93%, while the yield of 1:1 addition products was 73%. The yield of low-boiling products was 17%. Infrared analysis of the major products indicated 70% liquid isomer and 30% solid isomer. A gas chromatogram of the liquid isomer indicated a 5% yield of the 1-chloro-2-trichloromethylcyclooctane.

The distribution of minor products was quite similar to the other photo-initiated reaction and is summarized in Table II. The yield of hexachloroethane in this reaction

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*The use of benzene solvent to improve the efficiency of photolysis of CCl_4 was suggested by Professor G. W. Griffin of Tulane University.

was 0.89% compared to 0.07% for both the thermal and the photo-reaction without the benzene solvent.

H. Photo-initiated Addition of Bromotrichloromethane to cis-Cyclooctene

A solution of 30 g. of cyclooctene (0.27 mole) and 50 g. of freshly distilled $BrCCl_3$ (0.25 mole) in a Pyrex test tube was irradiated with a 3500 Å light source for four hours. The mixture was then distilled at reduced pressure to yield the following fractions:

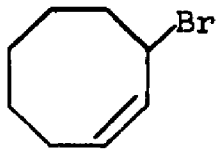
I	Dry Ice trap, 33 g. (the density of this material was 1.54, corresponding to 7 g. of cyclooctene (d_4^{20} = 0.85) and 26 g. of CCl_3Br (d_4^{15} = 1.96)).
II	60-70° @ 0.8 mm. 5 g.
III	70-90° @ 0.8 mm. 7 g.
IV	90-110° @ 0.8 mm. 7 g.
V	110-130° @ 0.8 mm. 19 g.

Fractions II, III, and IV were combined and distilled at 0.3 mm. to give four fractions: 1', 2', 3', and 4' (b.p. 50-70°, 16 g.). The residue (1 g.) from this distillation was mixed with V and distilled to give fractions 5', 6', and 7'.

5'	90-95° @ 0.6 mm. 3.5 g.
6'	101-110° @ 0.6 mm. 4 g.
7'	111-114° @ 0.6 mm. 9 g.

Gas chromatographic analysis indicated that 1', 5', and 7' were essentially pure samples of the three major

products described below. Fraction 1' gave two principle components (87 and 9%) and three minor ones (4%). The retention times of these five components were quite similar and suggest that they contain one bromine per C_8 group. The n.m.r. spectrum of this material, summarized below, suggests that the major component is 3-bromocyclooctene.



-5.75 p.p.m.	(1.8 protons, due to the vinyl hydrogens) The signal is unsymmetrical, indicating that the two vinyl hydrogens are non-equivalent.
-4.85 p.p.m.	(1 proton, $\underline{H}$-C-Br)
-2.15 p.p.m.	(4 protons, $C\underline{H}_2$-CH=CH and $C\underline{H}_2$-C-Br)
-1.65 p.p.m.	(6.2 protons, CH_2-$C\underline{H}_2$-CH_2)

On treatment with cold alcoholic $AgNO_3$, 1' gave an immediate precipitate, indicating an allylic bromide.

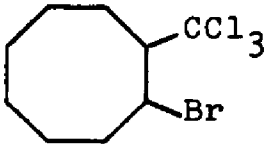
The minor component in 1' is probably bromocyclooctane. Its retention time is slightly longer than 3-bromocyclooctene, (same order as observed for 3-chlorocyclooctene and chlorocyclooctane). Also, the integrated vinyl hydrogen absorption is less than two protons, indicating that the other component is saturated.

Fraction 5' was identified as trichloromethylcyclooctane by comparison of its n.m.r. and infrared spectra with those of the authentic material.

Fraction 7' consisted of at least two isomeric $C_9H_{14}Cl_3Br$ products.

Anal. Calc. for $C_9H_{14}Cl_3Br$: C, 35.10; H, 4.57. Found: C, 35.01; H, 4.67.

The n.m.r. spectrum indicated that the major product was 1-bromo-2-trichloromethylcyclooctane (90%) and that the minor product was a 1,4 product or the cis-trans mixture of 1,4 products.



-4.85 p.p.m.	(0.9 proton, Br-C-H) consists of two triplets of equal intensity (J = 5 c.p.s) spaced 16 c.p.s. apart.
-4.25 p.p.m.	(0.1 proton, Br-C-H in 1,4 isomer)
-2.85 p.p.m.	(1.0 proton, H-C-CCl_3) This absorption is a complex multiplet of six peaks.
-2.1 p.p.m.	(4.4 protons, H_2C-C-X; X = Br, CCl_3)
-1.65 p.p.m.	(7.6 protons, H_2C-CH_2-CH_2)

Several features of this spectrum suggest a 1,2-disubstituted cyclooctane rather than a transannular product:

(1) The multiplicity of the H-C-Br and H-C-CCl_3 absorptions approximates two triplets which

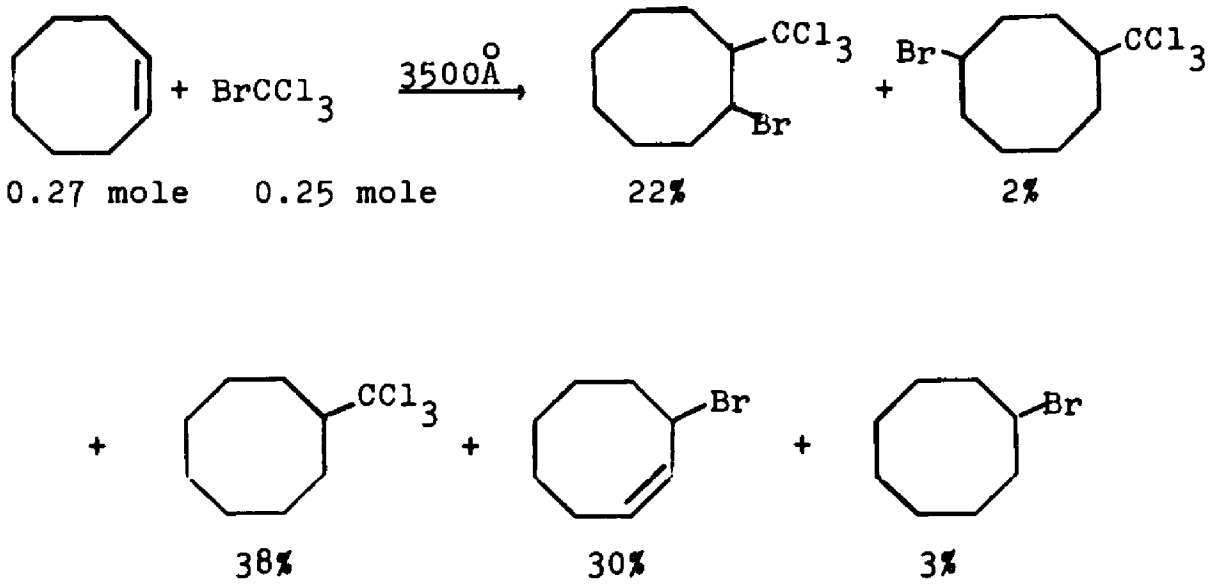
would be expected for the 1,2 isomer. The 1,4 isomer would be expected to give a quintet.

(2) The H-C-Br and H-C-CCl_3 absorptions are shifted downfield from their expected positions (-4.85 vs -4.25 and -2.85 vs -2.6), indicating an additional deshielding effect of a neighboring electron withdrawing group.

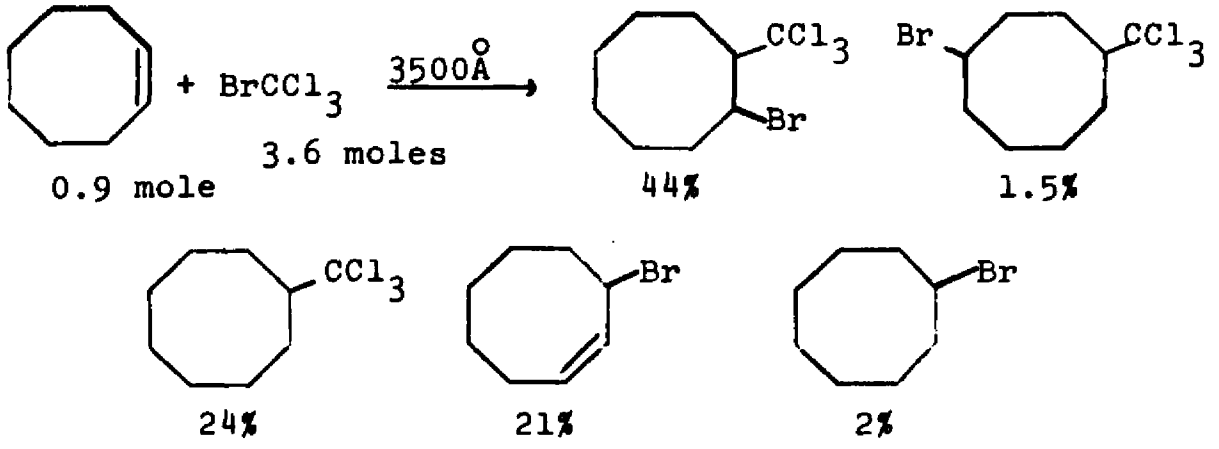
(3) The ratio of protons which absorb at -2.2 p.p.m. to those at -1.65 p.p.m. is consistent only with the 1,2 isomer.

The conversion of cyclooctene to products was 67% and the yield of 1:1 addition products was 24%.

Summary:



In a larger scale reaction utilizing excess $BrCCl_3$, the following yields were obtained:



Other N.m.r. Experiments.[48] In the discussion above, the chemical shift of the H-C-Br proton is given as -4.85 p.p.m. This figure is the average value for the two triplets at -5.00 p.p.m. and -4.70 p.p.m. (this chemical shift difference is equal to 18 c.p.s. at 60 m.c.). However, when the spectrum is obtained at 100 megacycles, the separation of these two triplets increases to 29 c.p.s. (0.29 p.p.m.) but the chemical shifts remain unchanged. At 100 megacycles, the H-C-CCl_3 signal also changes from the complex multiplet at -2.85 observed at 60 m.c. into two separate absorptions at -2.90 and -2.75 p.p.m.

These data are strong evidence that two different chemical species are responsible for these absorptions since the separation between component parts of the multiplet signal from the H-C-Br is dependent on field strength.[21]

The spin decoupling experiments which were run on this mixture prove unequivocally that it is a cis-trans mixture of 1-bromo-2-trichloromethylcyclooctanes. Irradiation of the absorption at -5.00 p.p.m. caused the split triplet at -2.75 p.p.m. to become a simple triplet but did not affect the absorption at -2.90 p.p.m. Similarly, irradiation of the peak at -4.70 p.p.m. caused the poorly resolved quartet at -2.90 p.p.m. to become a broad doublet but had no effect on the absorption at -2.75 p.p.m. These data allow no other explanation but the assumption of a cis-trans mixture of 1,2 isomers. The absorptions at -5.00 p.p.m. and -2.75 p.p.m. are due to the $\underline{H}$-C-Br and $\underline{H}$-C-CCl_3 protons in one isomeric pair, which are necessarily on adjacent carbons due to their coupling. The extension of this argument to the other pair of absorptions is immediate.

When the signal at -2.3 p.p.m. ($\underline{H}_2$C-C-Br) was irradiated, the signal at -4.70 p.p.m. became a broad doublet (J approximately 7 c.p.s.). Irradiation at a very slightly different position in the region of -2.3 p.p.m. ($\underline{H}_2$C-C-Br in the other isomer) caused the signal at -5.00 p.p.m. to become a broad singlet. This latter signal is most probably an unresolved doublet with J = 2 c.p.s., since this coupling constant had been measured independently and found to be 2 c.p.s. (recall that irradiation of the -5.00 p.p.m. peak caused the -2.70 p.p.m. to change from a

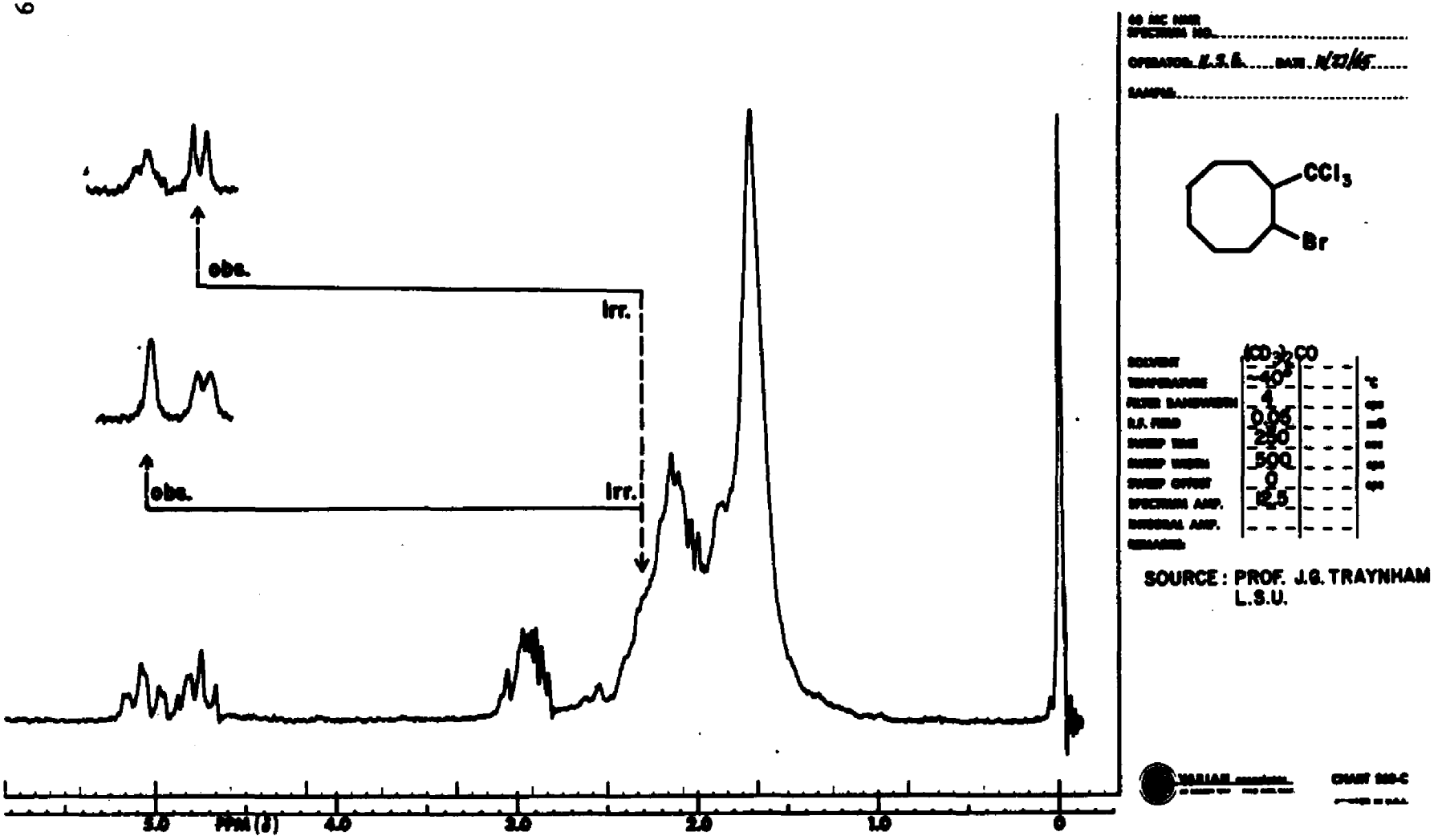


Fig. 1. Proton Decoupling Experiments on 1-Bromo-2-trichloromethylcyclooctane in Acetone-d_6.

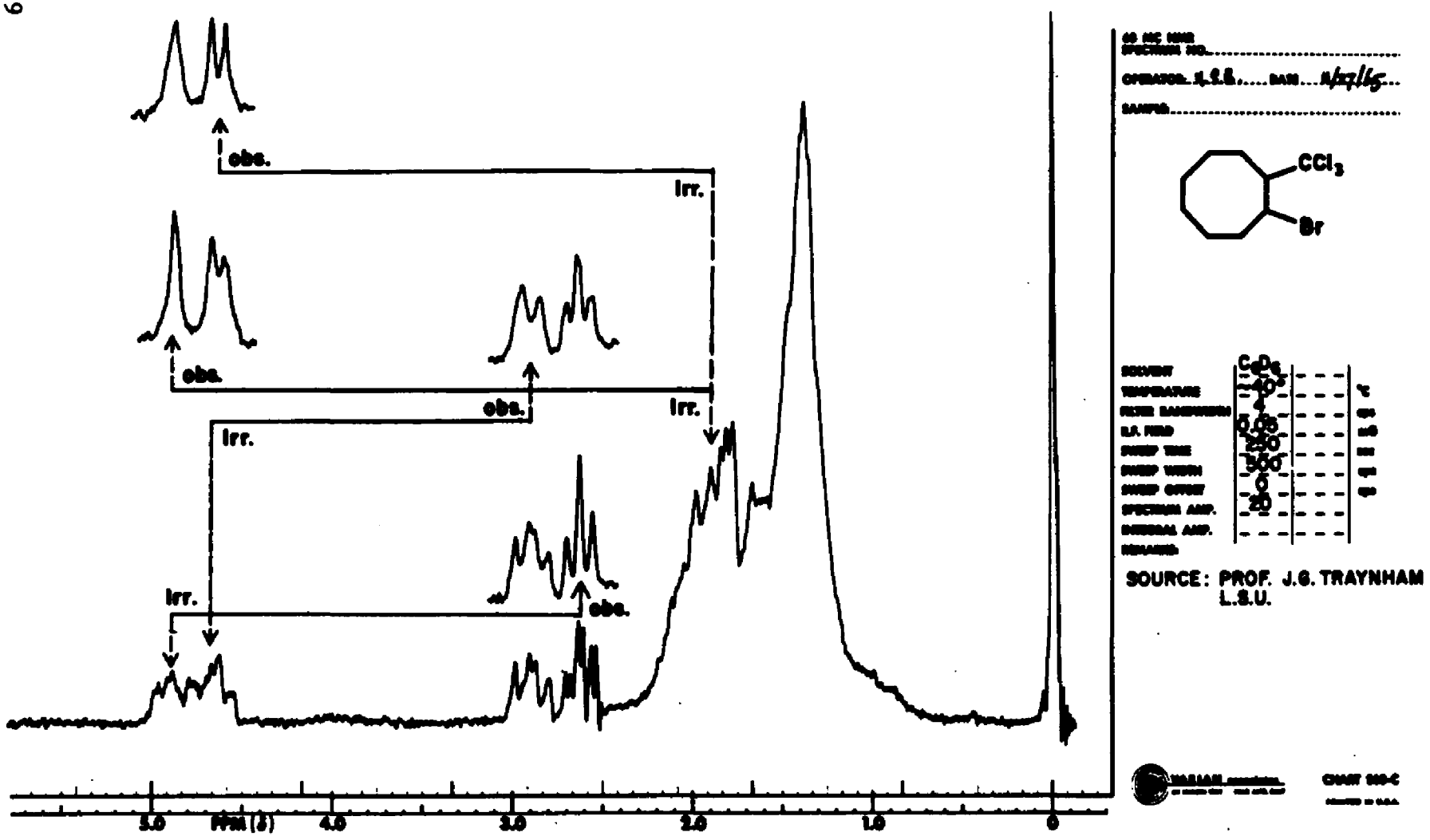


Fig. 2. Proton Decoupling Experiments on 1-Bromo-2-trichloromethylcyclooctane in Benzene-d_6.

split triplet to a simple triplet; the coupling which disappears is, by symmetry, the coupling of interest).

These data allow the assignment of the pair of absorptions at -5.00 and -2.70 p.p.m. to the cis isomer. The small coupling between the H-C-Br and H-C-CCl_3 protons, and the downfield position of the former with respect to the trans isomer, suggest that the bromine is in an axial-like position and that the trichloromethyl group is in an equatorial-like position in the preferred conformation (therefore cis). The relatively large coupling constant observed for the analogous protons in the other isomer is consistent with the assumption that the two large groups occupy equitorial-like positions (trans isomer).

A pronounced solvent effect on both the chemical shifts and the coupling constants was noted for this mixture, with the largest effect being noted for the cis isomer. As the solvent polarity was increased, (benzene-d_6, chloroform-d_1, acetone-d_6 and dimethyl sulfoxide-d_6) the H-C-CCl_3 proton in the cis isomer was shifted downfield, while the analogous proton in the trans isomer was unaffected. In DMSO-d_6, both the cis and trans isomer absorb at -2.90 p.p.m.

One explanation for this effect would be a specific solvation of the H-C-CCl_3 proton in the cis isomer with deshielding due to the proximity of the deshielding portions of the solvent molecules.[49] The merit of this suggestion,

rather than the suggestion of a conformational change, is that the H-C-Br proton is only slightly affected by a change in solvent polarity; a change in the conformation of the CCl_3-carbon would demand a change in the conformation of the Br-carbon accompanied by a shift (presumably downfield) of the H-C-Br proton absorption.

Examination of models of the cis and trans isomers suggests that the H-C-CCl_3 proton in the cis isomer should be more accessible to the solvent molecules since this proton bears a trans relationship to the relatively large bromine atom.

I. Perioxide-initiated Addition of Trichloromethanesulfonyl Chloride to cis-Cyclooctene

A solution containing 100 g. (0.45 mole) CCl_3SO_2Cl (Eastman Practical grade, used as received) in 150 ml. benzene was refluxed at 82° for 30 minutes. To this refluxing solution was added over 1.5 hours a benzene solution of 38 g. (0.35 mole) cyclooctene and 8 g. (0.04 mole) benzoyl peroxide. Titration of the evolved SO_2 with iodine indicated that 38% of the CCl_3SO_2Cl had decomposed in the first 30 minutes. The mixture was refluxed for 15 hours to ensure complete decomposition of the peroxide. A gas chromatogram of the reaction mixture before distillation showed two principal peaks (85%) of relative area 30:70 and at least eighteen minor components. Unreacted CCl_3SO_2Cl (4 g.) was

removed by vacuum sublimation, and the residue was distilled at reduced pressure to yield the following fractions:

I	35-90°	@ 0.48 mm., 5 g.
II	90-110°	@ 0.48 mm., 17 g.
III	110-111°	@ 0.48 mm., 17 g.
IV	111-114°	@ 0.48 mm., 40 g.

Fractions II, III, and IV were essentially free of low-boiling products, while I contained about 20% of the $C_9H_{14}Cl_4$ product. The recovered yield was 75 g. (81%); conversion of cyclooctene was greater than 96%.

N.m.r. analysis of II, III, and IV indicated that the minor $C_9H_{14}Cl_4$ product was the 1,2 isomer. The proportion of 1,2 isomer could be calculated from the integrated n.m.r. spectra by two different methods and compared with the results of gas chromatographic analysis. The description of these three methods and the results are summarized below.

(1) The 1,2 and 1,4 isomers are resolved by gas chromatography at 140° on the 100' GE-96 column provided a small sample of the mixture (0.2 ul. of a 30% solution in petroleum ether) is injected.

(2) The integrated absorption at -4.75 p.p.m. (1,2 isomer) was compared to the absorption at -4.25 p.p.m. (1,4 isomer).

(3) Comparison[16] was made of the integrated absorption to the left and right of -1.83 p.p.m. The 1,2

isomer gives a 5:8 distribution and the 1,4 isomer gives a 9:4 distribution.

	% 1,2 isomer		
Fraction	Method(1)	Method(2)	Method(3)
I	41±1	40±2	41±2
II	--	35	35
III	20	19	19

The infrared spectrum of fraction IV gave evidence that both the liquid and solid 1,4 isomers were present. Fractions II, III, and IV were recombined and dissolved in 150 ml. pentane. On cooling to -50°, the solid 1,4 isomer separated from the other two isomers. Fractional crystallization from pentane (-30°) led to the isolation of 16 g. of the solid 1,4 isomer. The melting point was 64.5-65°, and a mixed melting point with the previously prepared solid 1,4 isomer showed no depression. The combined pentane solutions were cooled to -70° for several hours, yielding an additional 0.5 g. of crystalline material, and finally decanted. The solvent was removed from the liquid layer and gave 53 g. of $C_9H_{14}Cl_4$ product (39% 1,2 isomer).

The liquid 1,4 isomer (b.p. 109° @ 0.5 mm.) and the 1,2 isomer (b.p. 104° @ 0.5 mm.) could not be separated by simple distillation; however, 5 distillations through a 12" packed column with an 8" Vigreux head led to the separation of the 1,2 isomer in 77% purity and the 1,4 isomer in 86% purity.

The identity of the 1,4 liquid isomer was confirmed by comparison of its n.m.r. and infrared spectra with the previously identified material.

The n.m.r. spectrum of 1-chloro-2-trichloromethylcyclooctane is almost identical to the spectrum of 1-bromo-2-trichloromethylcyclooctane. The one proton absorption due to H-C-Cl is a pair of triplets (J = 5.5 c.p.s.) separated by 18 c.p.s. at -4.75 p.p.m. The ratio of protons at 2.2 p.p.m. to those at -1.65 p.p.m. was 5:8 (after correction for 23% 1,4 isomer).

Anal. Calc. for $C_9H_{14}Cl_4$: C, 40.94; H, 5.35. Found: C, 41.39; H, 5.51.

The infrared spectrum of the 1,2 isomer was similar to the spectra of the two 1,4 isomers in the 7-11 μ region. The carbon-chlorine stretching frequency for the 1,2 isomer was observed at 690 $cm.^{-1}$, compared to 675 $cm.^{-1}$ and 672 $cm.^{-1}$ for the liquid and solid 1,4 isomers, respectively.

1. Dehydrochlorination of 1-Chloro-2-trichloromethylcyclooctane

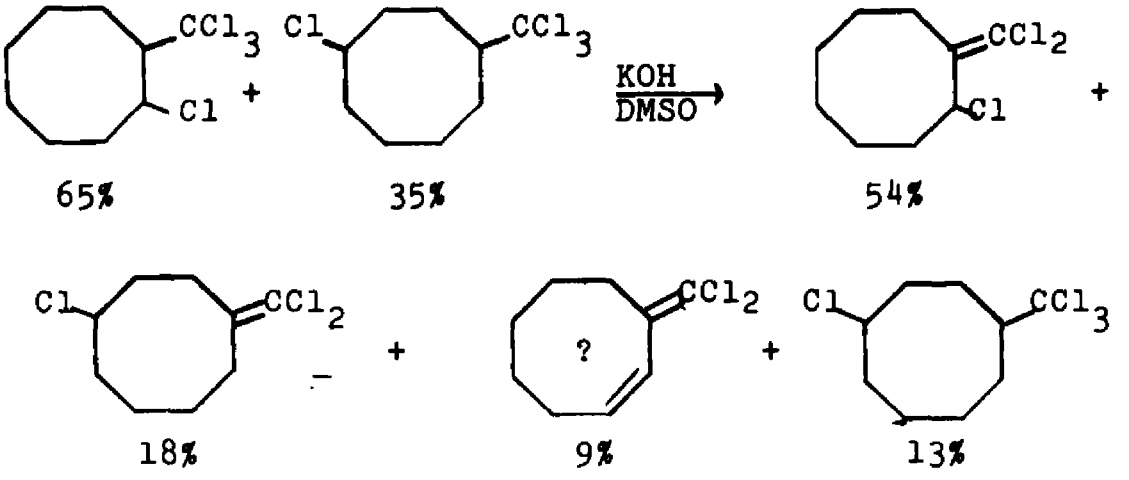
Because of the remarkable selectivity of KOH and $AgNO_3$ in the dehydrochlorination of the 1,4 isomers, a preliminary study of the reaction of these reagents with the 1,2 isomer was made. This work is incomplete at present; however, the available results will be given here.

a. KOH in DMSO-MeOH

To a solution of 4.4 g. of mixed $C_9H_{14}Cl_4$ isomers (65% 1,2 isomer, 35% 1,4 isomer, 0.0160 mole) in a mixed solvent (5 ml. of MeOH, 35 ml. of DMSO) was added (at room temperature) 1.1 g. of KOH in 18 ml. of DMSO-MeOH-H_2O (10:5:3) solvent. After six hours of stirring, the mixture was poured into water. The work-up was similar to that previously described for the analogous reaction with the 1,4 isomer and yielded 3 g. of product after removal of solvent. The gas chromatogram of this mixture showed five peaks of relative ratio (in order of increasing retention time) 9:5:54:18:13. The last two have retention times identical to 1-chloro-4-dichloromethylenecyclooctane and the unreacted 1-chloro-4-trichloromethylcyclooctane, respectively. The peak corresponding to the 1,2 isomer was apparently absent.

The major component (54%) had a retention time suggesting three chlorines. The infrared spectrum of the mixture gave only trace absorption for vinyl hydrogen, but gave intense bands at 6.23 μ and 11.02 μ for the $C{=}CCl_2$ grouping.[33] The $-CCl_3$ absorption was weak and probably due to unreacted $C_9H_{14}Cl_4$. Since 1-chloro-4-dichloromethylene-cyclooctane absorbs at 11.10 μ, the band at 11.02 μ is probably due to the major component. These data allow tentative assignment of the structure of the major product

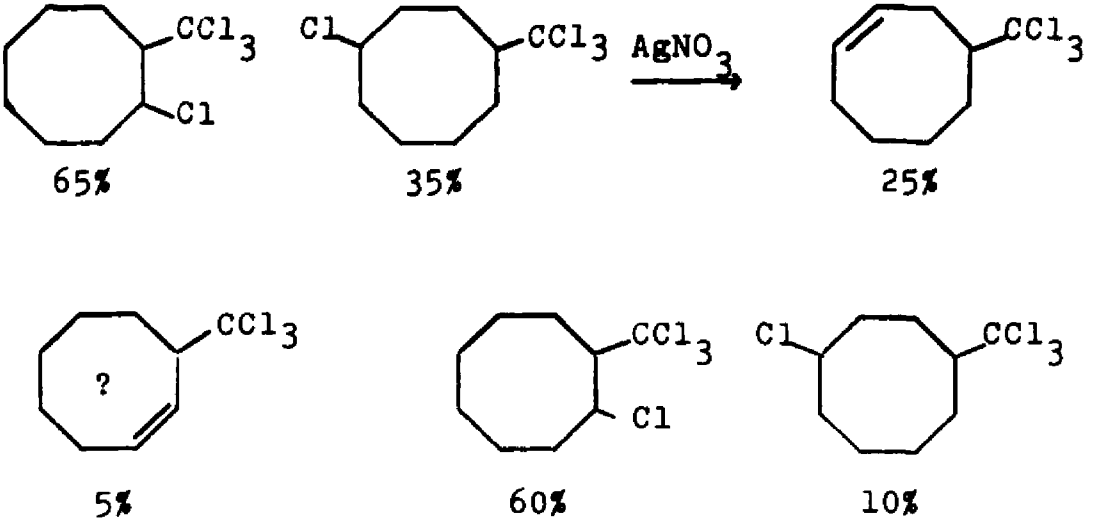
as 1-chloro-2-dichloromethylenecyclooctane. The retention time of the first product suggests two chlorines. Loss of HCl from the major product would give the conjugated 3-dichloromethylenecyclooctene. The 1,2 isomer may be estimated to react 10-100 times faster than the 1,4 isomer under these conditions.



<u>$AgNO_3$ in Aqueous MeOH</u>

A solution of 3.6 g. $C_9H_{14}Cl_4$ mixture (0.0136 mole, 65% 1,2 isomer) and 2.47 g. $AgNO_3$ (0.0166 mole) in 50 ml. of 90% methanol was refluxed for five hours. The mixture was filtered and poured into water. Work-up was similar to previous silver nitrate dehydrochlorinations and yielded 3 g. of a product mixture after removal of solvent. Gas chromatographic analysis showed only three important peaks of relative area 25:5:70. The largest peak is unreacted $C_9H_{14}Cl_4$ and was nearly pure 1,2 isomer. The next largest peak had a retention time identical with that of

4-trichloromethylcyclooctene. The intermediate peak might be expected 3-trichloromethylcyclooctene, judging from its retention time; however, no other data are available. In contrast to the relative rates of basic dehydrochlorination, the 1,4 isomer apparently reacts much faster with $AgNO_3$ than the 1,2 isomer. This fact offers promise as a method of separating the positional isomers, although this line was not pursued.



J. Photo-initiated Addition of Chloroform to cis-Cyclooctene

Freshly distilled cyclooctene (42 g., 0.38 mole) was mixed with $CHCl_3$ (360 g., 3.0 moles) in a 300 ml. quartz tube. Nitrogen was used to deoxygenate the mixture for 15 minutes and a nitrogen stream was slowly passed over the mixture during illumination and directed into a 10% NaOH solution to absorb any HCl or Cl_2 formed in the reaction.

After 65 hours of illumination (2537 Å light), the excess $CHCl_3$ was removed by rotary evaporation and the residue was distilled under reduced pressure. This procedure afforded 35 g. of unreacted cyclooctene and 8 g. of higher boiling material. A gas chromatogram of the product mixture showed three peaks of relative area 15:55:30 in order of increasing retention time.

The lowest boiling product (b.p. 40-42° @ 0.6 mm.) was separated from the other two products by distillation. The n.m.r. spectrum of this material included a well resolved quintet at -4.14 p.p.m. (J = 5.0 c.p.s., 1 proton) corresponding to H-C-Cl. Also noted were absorptions at -2.02 p.p.m. (CH_2-C-Cl, 4 protons) and -1.65 p.p.m. (CH_2-CH_2-CH_2, 10 protons). This product was shown to be chlorocyclooctane by comparison with an authentic sample (see p. 76).

The other two products were separated by preparative gas chromatography. The major component gave an elemental analysis for $C_9H_{16}Cl_2$.

Anal. Calc. for $C_9H_{16}Cl_2$: C, 55.39; H, 8.27. Found: C, 55.77; H, 8.29.

The infrared spectrum showed a band at 13.4 μ and no evidence for unsaturation. The n.m.r. spectrum showed a sharp doublet at -5.07 p.p.m. (1 proton, CH-$CHCl_2$, J = 3.0 c.p.s.). Other absorptions were -2.1 p.p.m. (1 proton, CH-$CHCl_2$) and -1.65 p.p.m. (14 protons, -CH_2-). These data indicate dichloromethylcyclooctane as the structure.

The third product was the expected trichloromethylcyclooctane and was identical to the product isolated from the CCl_4-cyclooctene and $CBrCl_3$-cyclooctene reactions. The elemental analysis, n.m.r. and infrared spectra have already been described. The recovered yields of these products were 1.5, 5.5, and 3%. Minor amounts of several other products were observed by chromatography. The NaOH solution used to trap gaseous products was neutralized with acetic acid diluted with distilled water. Treatment with $AgNO_3$ afforded 5.0 g. AgCl, indicating 1.6 g. (0.046 eqv.) of HCl and/or Cl_2 had been formed in the reaction. The following molar amounts of products were formed: HCl, 0.046 mole; trichloromethylcyclooctane, 0.013 mole; dichloromethylcyclooctane, 0.026 mole; and chlorocyclooctane, 0.0065 mole. Trace amounts of hexachloroethane (0.0005 mole), trans 1-2 dichlorocyclooctane (0.0001 mole) and dichloromethylenecyclooctane (0.0001 mole) were detected by gas chromatography, but were not isolated.

K. Preparation of Chlorocyclooctane and 3-Chlorocyclooctene

1. Chlorocyclooctane[45]

A stirred mixture of cyclooctene (10 g., 0.09 mole) and 0.5 g. of zinc dust in 40 ml. of benzene was treated with dry HCl until the solution was saturated. The solution was stirred for an additional hour and then washed once with water and once with 5% sodium bicarbonate solution. After

drying ($CaCl_2$) and concentration by rotary evaporation, gas chromatographic analysis indicated that 50% of the cyclooctene had been converted to a single product.

The gas chromatographic retention time of this sample of chlorocyclooctane was identical to that of the minor product isolated from the CCl_4 and $CHCl_3$ addition reactions (see pp. 53 and 75, respectively). The n.m.r. spectrum of chlorocyclooctane has been described (p. 75).

2. 3-Chlorocyclooctene

To a 3 neck flask equipped with a magnetic stirrer, dropping funnel and reflux condenser, was added 10 g. (0.074 mole) of 2-cycloocten-1-ol.[32] The reaction flask was maintained at 0-10° by means of a surrounding ice bath. Thionyl chloride (25 g., 0.21 mole) was added dropwise to the neat alcohol over a period of 45 minutes. After an additional hour of reaction, the excess thionyl chloride was carefully hydrolyzed with ice. The resulting mixture was added to 100 ml. of petroleum ether and the layers were separated. The aqueous layer was extracted once with petroleum ether, and the combined organic layers were washed twice with water. The solution was dried over magnesium sulfate and concentrated by rotary evaporation. Gas chromatographic analysis indicated essentially quantitative conversion to a single product. The retention time of this sample of 3-chlorocyclooctene was identical to that of the

product isolated from the addition of CCl_4 to cyclooctene (p. 53).

L. Chlorination of cis-Cyclooctene[23]

1. Free Radical Conditions

Cis-cyclooctene was refluxed over sodium for 18 hrs. and then distilled. A constant boiling fraction (50 ml.) was collected and immediately flushed with nitrogen. Approximately 25 g. of chlorine was condensed in a Dry Ice trap. Nitrogen gas was then passed over the liquid chlorine for several minutes to remove dissolved oxygen. The liquified chlorine was allowed to vaporize slowly in a stream of nitrogen (-40°) as the mixture of gases was bubbled into the cyclooctene. The Pyrex reaction vessel was immersed in a beaker of water and illuminated with a 100 watt lamp placed three inches from the beaker. A gas chromatogram of the resulting mixture revealed an 89% yield of dichlorocyclooctanes, 7% of 3-chlorocyclooctene and 4% of a product of slightly lower retention time. The principal product was collected at $78-80^{\circ}$ (1.5 mm.).

Anal. Calc. for $C_8H_{14}Cl_2$: C, 53.05; H, 7.79. Found: C, 53.16; H, 7.95.

Gas chromatography revealed the presence of a minor $C_8H_{14}Cl_2$ isomer (6%) in addition to the principal product. The major isomer was identified as trans-1,2-dichlorocyclooctane by comparison of its infrared spectrum with the

reported[23c] spectrum. Characteristic bands were noted at 612, 663, 737, and 783 cm.$^{-1}$. The n.m.r. spectrum was consistent with a 1,2-disubstituted cyclooctane, giving an 8 proton absorption at -1.65 p.p.m. and a 4 proton absorption at -2.13 p.p.m. A 2 proton absorption was also noted at -4.21 p.p.m. for the H-C-Cl grouping. The dichloro-compounds were converted in a 90% yield to cis-cyclooctene by refluxing (135°) for 24 hours with zinc dust in ethylene glycol monoethyl ether ("Cellosolve"). No unreacted dichlorocyclooctanes were recovered; the remainder of the product mixture was composed of three compounds whose retention times suggested 1 chlorine per 8 carbon atoms. Refluxing with excess potassium iodide for 24 hours in Cellosolve gave a 25% conversion to cis-cyclooctene.

2. Ionic Conditions

A solution of 45 g. cyclooctene in 125 ml. chloroform was continuously saturated with air by means of a gas dispersion tube. A chlorine generator was prepared from a three neck 500 ml. flask equipped with a pressure regulating funnel and a gas outlet tube. Chlorine, generated by dripping 58 g. of concentrated HCl (37%) on 28 g. potassium permanganate, was passed into the solution at a rapid rate. After addition was complete (30 minutes) the solvent was removed and a gas chromatogram taken. The yield of dichlorocyclooctanes determined by gas

chromatography was 90%, of which 88% was trans-1,2-dichlorocyclooctane and 2% was the unidentified isomer mentioned previously. The other products were 3-chlorocyclooctane (5.5%) and a compound of slightly lower retention time (same as before, 4.5%). The major product, collected at 78-80° @ 0.8 mm.,[50] was shown to be identical to the product from the free radical reaction by comparison with its infrared and n.m.r. spectra. This product was also converted to cis-cyclooctene by treatment with either zinc dust or potassium iodide in refluxing Cellosolve.

M. Chlorination of cis-Cyclodecene[32]

1. Free Radical Conditions

Cis-cyclodecene (17 g., 95% purity) was freshly distilled from sodium and placed in a test tube fitted with a two hole rubber stopper. Approximately 14 g. of chlorine was condensed in a Dry Ice trap and flushed with nitrogen for several minutes. The chlorine was allowed to vaporize in the nitrogen stream (-40°) and passed into the neat cyclodecene. After addition was complete, a gas chromatogram of the mixture showed an 85% yield of $C_{10}H_{18}Cl_2$ products and a 10% yield of a mixture (poorly resolved) of compounds whose retention times suggested 1 chlorine per 10 carbons. The principal product was collected at 93-95° @ 0.65 mm. (21 g., 75% yield isolated).

Anal. Calc. for $C_{10}H_{18}Cl_4$: C, 57.42; H, 8.67. Found: C, 57.37; H, 8.74.

The n.m.r. spectrum gave the expected distribution for the 1,2 product: -4.38 p.p.m. (2 protons, H-C-Cl), -2.09 p.p.m. (4 protons, CH_2-C-Cl) and -1.69 p.p.m. (12 protons, CH_2-CH_2-CH_2). The band at -4.38 p.p.m. was unsymmetrical and quite complex (12 lines under high resolution) in contrast to the analogous spectrum of trans-1,2-dichlorocyclooctane.

2. Reaction of 1,2-Dichlorocyclodecane with Zinc Dust

The above product was refluxed (135°) in 100 ml. Cellosolve with 10 g. of zinc dust for six hours. Gas chromatography revealed a 97% conversion of the dichloro-compound to a mixture of 61% trans-cyclodecene and 39% cis-cyclodecene. The trans-cyclodecene was identified by comparison of its infrared spectrum and gas chromatographic retention time with an authentic sample.[51] The spectrum included a strong band at 10.21 μ, characteristic of trans-cycloalkenes.[52]

3. Ionic addition

A solution of 10 g. cyclodecene in 250 ml. CCl_4 was placed in a 50 ml. Erlenmeyer flask. Approximately 6 g. of chlorine was condensed in a Dry Ice trap, allowed to vaporize in a stream of oxygen, and passed into the cyclodecene solution by means of a fritted-glass dispersion

tube. After addition was complete the solvent was removed by rotary evaporation and a gas chromatogram was taken. The chromatogram revealed a 93% yield of a dichloro-compound and only one monochloro product. The principal product was collected at 96-97° @ 0.70 mm. (13 g., 87% recovered yield). The infrared and n.m.r. spectra of this material were identical to those for the product obtained under free radical conditions. Dechlorination in Cellosolve with zinc dust led to 95-98% conversion to a mixture of 61% trans cyclodecene and 39% cis-cyclodecene. Dechlorination with potassium iodide in Cellosolve for 50 hours led to an 88% conversion of the dichloro-compound to a mixture of 79% trans-cyclodecene and 21% cis-cyclodecene. At 10% conversion, the mixture was 76% trans and 24% cis, while at 60% conversion, the ratio was 71:29.*

N. Photo-initiated Addition of Carbon Tetrachloride to cis-Cyclodecene

A solution of freshly distilled cis-cyclodecene (20 g., 0.145 mole) in reagent grade carbon tetrachloride (370 g., 2.5 moles) was placed in a quartz flask and deoxygenated by a nitrogen stream for ten minutes. The flask was

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*Stevens and Valicenti (ref. 24) have demonstrated that debromination by zinc is less stereoselective than by potassium iodide. Their potassium iodide debromination was 100% trans.

irradiated (2537 Å light) in a nitrogen atmosphere for 36 hours. A cooling fan kept the reaction mixture at 44°.

The excess CCl_4 was removed by rotary evaporation. The residue (37.5 g.) was distilled at reduced pressure, the following fractions being obtained:

I	53-62°	@ 2.4 mm.	5.8 g.
II	62-100°	@ 2.7 mm.	2.0 g.
III	100-120°	@ 2.7 mm.	5.6 g.
IV	120-155°	@ 3.5 mm.	8.0 g.
V	residue		12.0 g.

Gas chromatography revealed that fraction I was mainly unreacted cyclodecene, while fraction II contained a complex mixture of chlorocyclodecenes, similar to that obtained from the free radical chlorination of cyclodecene.

The gas chromatographic retention times of the principal components of III and IV suggested two chlorines per C_{10} or C_{11} group. The infrared spectra of III and IV were devoid of the intense absorption due to $-CCl_3$, but contained the characteristic $C{=}CCl_2$ absorptions at 6.2 and 11.1 μ. These two fractions were dissolved in pentane and cooled to -50°. This caused the separation of 1.0 g. of a solid material (m.p. 102-104°) whose analysis indicated $C_{10}H_{18}Cl_2$.

Anal. Calc. for $C_{10}H_{18}Cl_2$: C, 57.42; H, 8.67. Found: C, 57.32; H, 9.05.

The n.m.r. spectrum indicated a transannular C_{10}-dichloride (probably trans-1,6)[54] and had the following features: -4.20 p.p.m. (2 protons, H-C-Cl). This absorption is a well formed quintet with J = 5.7 c.p.s.

-2.0 p.p.m. (8 protons, CH_2-C-Cl),

-1.7 p.p.m. (8 protons, CH_2-CH_2-CH_2).

The n.m.r. spectrum of the liquid fraction showed only trace absorption at -4.2 p.p.m. for H-C-Cl. On this basis, and from the consideration of the infrared spectra mentioned before, the principal product is probably dichloromethylenecyclodecane (63% yield). The residue (V) was dissolved in pentane and cooled to -50° for several hours. No crystalline products were obtained by this procedure, and this fraction was not examined further.

If any 1:1 addition products were formed in this reaction, their boiling points were too high for the pressure obtained during distillation.

CHAPTER IV

SUMMARY

Free radical additions to medium ring olefins proceed through an intermediate 2-substituted-cycloalkyl radical which may react by several paths, depending on their relative free energy requirements. The transannular hydrogen migration appears to have a rather high activation energy compared to that for the chain transfer step but is able to compete with normal addition because of a very favorable entropy of activation.

In contrast to most olefins, polymerization is relatively unimportant in these systems. The importance of other competing reactions, such as allylic substitution, is difficult to assess. The addition of bromotrichloromethane to cyclooctene gives 25-50% yields of addition product with allylic attack predominating. The allylic attack in this case apparently involves attack by a bromine atom rather than the trichloromethyl radical. The high yield of 3-bromocyclooctene results from the ability of the relatively stabilized allylic radical to abstract bromine from bromotrichloromethane.

In this work, only 1,2- and 1,4-disubstituted products were found. The 1,4 product arises from an overall 1,5

hydrogen shift (from atom 4 to atom 8). While 1,3 or 1,4 shifts should be possible, they apparently cannot compete with 1,5 hydrogen shift due to higher energy requirements.[54] Examination of models indicates that only 1,5 migration can procede through a transition state in which the hydrogen being abstracted is nearly collinear with the 1 and 5 carbon atoms. This geometrical arrangement allows maximum orbital overlap of the bond being formed with the bond being broken, considerably lowering the activation energy for the process.

More work is needed in these system before it will be possible to predict the mode of addition for a new addend. If the kinetic parameters for the transannular hydrogen shift could be determined with accuracy, a reasonable prediction of the mode of addition could be made from the bond dissociation energies and chain transfer constants for the various addends.

The scope of this experimental work was the isolation and identification of the products formed. Determination of the kinetic parameters would require that the reactions be run to low conversion with careful control of temperature, concentration, and rate of initiation. In addition, better analytical techniques would be required to determine the yield of the minor addition products.

Several important features of these addition reactions remain unexplained. Two transannular isomers are formed in

the addition of CCl_4 to cyclooctene. While the cis-trans relationship of these isomers has been established, the available data do not allow definite assignment of stereochemistry to each isomer. The proportion (2:1) of these two isomers was nearly constant over a wide range of experimental conditions. The 4-trichloromethylcyclooctyl radical probably exists long enough to undergo a conformational equilibration between the odd electron and the hydrogen on carbon 4. The product distribution would depend on the preferred direction of attack by the addend molecule. Work with the related 4-t-butylcyclohexyl radical suggests that chain transfer occurs with the odd electron in an axial position, leading to a 2:1 ratio of cis- to trans-1-chloro-4-t-butylcyclohexane.[55] This result would suggest that the liquid 1,4-$C_9H_{14}Cl_4$ isomer is cis; however, this assignment must be considered tentative in the absence of other data.

The stereochemistry of the 1,2-$C_9H_{14}Cl_4$ and the 1,2-$C_9H_{14}Cl_3Br$ addition products also requires additional study. The n.m.r. spectrum of the bromo-compound at 100 megacycles suggests two isomers of nearly equal abundance. The presence of both 1,2 isomers is less surprising than the fact that they are formed in equal amounts. The large trichloromethyl group would certainly control the stereochemistry of the intermediate radical, but the exact

description of the addition process requires more data. A 100 megacycle n.m.r. spectrum of 1-chloro-2-trichloromethylcyclooctane has not been obtained yet, but the 60 megacycle spectra of the chloro- and bromo-products are so similar that one may assume that both isomers are formed.

Much more work is needed in the cyclononene and cyclodecene systems. This work was concerned mainly with the study of cyclooctene, with only preliminary investigations of cyclodecene. The unusual stereochemistry of chlorine addition to cis-cyclodecene suggests that much additional information could be gained by the study of different ring sizes.

The author wishes to apologize if this work seems incomplete. Each result appeared to answer one question and suggest several new ones. Perhaps these questions are the real results of any research problem.

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VITA

Thomas Michael Couvillon was born in Baton Rouge, Louisiana, on December 17, 1940. He attended parochial school in that city and was graduated from Catholic High School of Baton Rouge in May of 1958. He entered Louisiana State University in September of 1958 and was awarded a Bachelor of Science degree from that institution in June, 1962.

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EXAMINATION AND THESIS REPORT

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Major Field: Chemistry (Organic Chemistry)

Title of Thesis: Free Radical Additions to cis-Cyclooctene and cis-Cyclodecene

Approved:

James G. Traynham
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